Thesis for the Degree of Ph.D.

The manner in which the rate of removal of halogen from halogenated benzenoid derivatives is governed by atoms or groups of atoms which repress reactivity.

by

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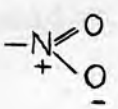
CONTENTS.

INTRODUCTION.

It is well known that when an atom or group enters the nucleus of a monosubstituted benzenoid derivative it does so at a position determined by the nature of the substituent already present. These substituents can be divided into two classes, namely, those which direct the entering atom, or group of atoms, into the ortho or para positions and those which direct the second substituent into the meta position. The hydroxyl and methyl groups, examples of the first class, render the ortho and para hydrogen atoms in the benzene nucleus to which they are attached more reactive than those in benzene, whilst the nitro and carboxyl groups, examples of the second class, render all the nuclear hydrogen atoms less reactive (than those in benzene) but leave the meta, and to a smaller extent the ortho hydrogen atoms still capable of being replaced by another substituent.

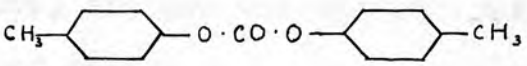
Recent work on the rate of removal of halogen by a hydrolysing agent (aqueous alcohol) (Olivier, Rec. trav. Chim. 1923, 42, 516) (Lapworth and Shoesmith J.C.S., 1922, 1391) from the $-CH_2(Hal.)$ group in a series of substituted benzyl halides has shown that there is a close connection between the ease of removal of this type of halogen, and the ease with which substituents enter a benzene nucleus, when the

same atom (or group of atoms) is present in the substituted benzyl halide and simple benzenoid derivative. The ease of removal of halogen in this way is dependent on its "negativity". This, in turn, results from the accumulation of electrons at this point, when its tendency to ionise is increased. The fact that the halogens in all the ω-bromoxylenes (Shoesmith and Slater, J.C.S., 1924, 125 2278) are more readily removed than is that from benzyl bromide points to the repulsion of electrons from the methyl group to the halogen atom. This is thereby rendered more negative and more readily detached by the positive hydrogen ion ($H^{\cdot}$) of the reagent. Sir J.J. Thomson, in experiments with the positive ray tube detected (CH_3+) but never (CH_3-). This is borne out by Lucas, Simpson and Carter (J.A.C.S., 1925, 47 1462-69) who say that in a substitution process the position of an entering substituent will be that at which electrons are least firmly held by carbon, and point out the difference in attraction for electrons between hydrogen (H) and the methyl group (CH_3). As a result of their experiments they came to the conclusion that the electrons were repelled from the (CH_3) group. On the other hand, the slow rate of hydrolysis of the nitrobenzylbromides (J.C.S., 1924, 125 1312) is due to the reverse effect, namely the attraction of electrons to the nitro group, a group which has been shown to contain one double bond and a semi-polar double bond

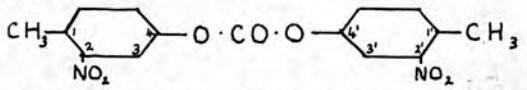


(Sugden and collaborators, J.C.S., 1925, 127 1525; Annual Reports Chem.Soc., 1926, 131) the positive end of which is on the nitrogen atom and attracts electrons from the benzene nucleus. The repulsion of electrons to, or withdrawal from the atoms attached to the nucleus, is responsible for the general polar effect (Lapworth and Shoesmith loc.cit.).

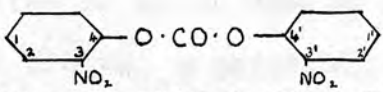
A noteworthy example of the nuclear position attacked by a nitro group when the nucleus already contains a methyl (CH_3) and protected hydroxyl group, was reported by Lucius and Brunig (Frdl., 1909, 9 151) who discovered that when di-p-tolylcarbonate of formula:-



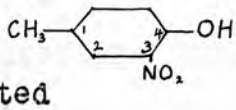
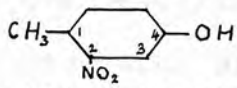
was subjected to the action of concentrated nitric acid, the main product was 2:2'-dinitro-di-p-tolyl-carbonate of formula:-



that is, the positions of attack were chiefly 2 and 2' (O.CO.O = 4). This was unexpected since, when Kempf (J.pr.Chem., 1870 (2) 1 407) subjected phenylcarbonate to the action of concentrated nitric acid the main product of reaction was 3:3' dinitrophenyl-carbonate of formula:-

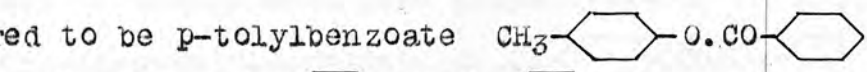
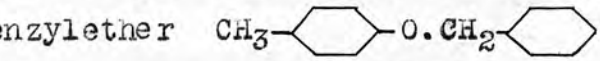
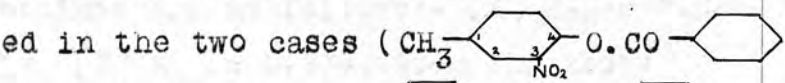
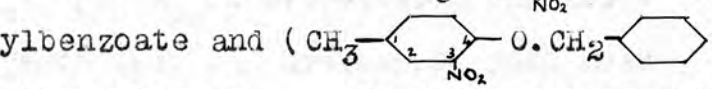


the chief positions of attack were 3 and 3' (O.CO.O = 4). Holleman and Hoeflake (Rec.trav.Chim., 1917, 36 271) repeated these experiments using a mixture of concentrated nitric acid and 100% sulphuric acid and

estimated accurately the products formed in the case of the di-p-tolylcarbonate. The dinitro-p-tolylcarbonates produced were hydrolysed with 4% aqueous caustic soda and the solution so obtained acidified with dilute sulphuric acid. On the passage of a current of steam through the acidified solution the 3-nitrocresol ($CH_3 = 1$) of formula:-  which is volatile in steam was separated quantitatively from the non-volatile 2-nitrocresol ($CH_3 = 1$) of formula:-  The ratio of the 1:3:4 to 1:2:4 compound was found to be 3:7 : 96.3. In this reaction, therefore, it is the methyl group and not the hydroxyl which determines the position of attack.

The neutralisation of the influence of the oxygen atom can be explained in two ways; a steric or spatial effect of one benzene nucleus on the other, or the general polar effect of the carbonyl group ($>C=O$) which is responsible:- (i) for the slow hydrolysis of the ω-bromotoluic acids (J.C.S., 1924, 125 1312) (ii) the difficulty in bringing about substitution in the nucleus of benzoic acid. The withdrawal of electrons from the nucleus by the ($>C=O$) group is considered as being due to the fact that it acts as a dipole $>\overset{+}{C}=\overset{-}{O}$, a point which has recently been mentioned in Ann.Reports Chem.Soc.,1929,p.131. Experiments were carried out to determine the extent to which the entrance of the substituent meta to the

singly bound oxygen atom※(-O-) is dependent on the group of atoms attached to this oxygen atom and how far it is influenced by steric or spatial effects.

The compounds most suitable for this purpose were considered to be p-tolylbenzoate  and p-tolylbenzylether  Attempts to nitrate these compounds by a method similar to that used by Holleman and Hoeflake (loc.cit.) for the nitration of di-p-tolylcarbonate only proved successful in the case of the p-tolylbenzylether since p-tolylbenzoate was hydrolysed with production of benzoic acid and cresol. The p-tolylbenzoate was successfully nitrated in glacial acetic acid solution. The nitro group in both cases entered the 3 position (CH_3 = 1) and compounds with the following formulae were identified in the two cases () 3-Nitro-p-tolylbenzoate and () 3-Nitro-p-tolylbenzylether. In these experiments it was the hydroxyl and not the methyl group which determined the position of attack. This did not give all the information required however because it was not found possible to nitrate the three compounds under the same conditions.

In view of the close connection which exists between substitution in the nucleus of benzenoid derivatives and hydrolysis of the corresponding substituted benzyl halides, a chlorine atom was introduced into the molecule of di-p-tolylcarbonate,

※ The symbol (-O-) is employed here and elsewhere to denote an oxygen atom directly attached to a nucleus.

p-tolylbenzoate and p-tolylbenzylether and the lability of this chlorine in the undermentioned compounds examined to see if further information could be gained as to the effect of the (>C=O.) (see graph 1, p. 14).

(A) ω-ω'-dichloro-di-p-tolylcarbonate. CH_2Cl-C$_6$H$_4$-OCO.O-C$_6$H$_4$-CH_2Cl,

(B) ω-chloro-p-tolylbenzoate, CH_2Cl-C$_6$H$_4$-O.CO-C$_6$H$_5$, and

(C) ω-chloro-p-tolylbenzylether, CH_2Cl-C$_6$H$_4$-O.CH_2-C$_6$H$_5$.

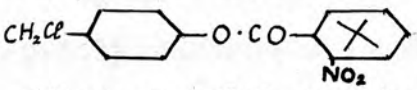
For comparative purposes the hydrolyses of the above compounds were carried out in 10% aqueous ethyl alcohol at 76°C. The hydrolysis of (C) was very rapid at this temperature and a second determination had to be made at 25°C. R_t is an approximate rate of hydrolysis and is the reciprocal of the time in hours required to hydrolyse 50% of the substituted benzylchloride. The results obtained are as follows:- (A) $R_{76°} = 0.235$. (B) $R_{76°} = 0.417$. (C) $R_{25°} = 0.934$. From the above results it is seen that (A) hydrolyses much more slowly than (B) or (C), which is in agreement with the results obtained in nitration experiments. The fact that (C) hydrolyses much more rapidly than (B) shows that the relaying of electrons from the hydroxyl group is a process which takes place more readily from the (O-CH_2) grouping than from the (O-C=O) group. (see pp. 8 & 9).

Experiments were carried out to determine what effect substituents, in the benzene nucleus of the benzoyl and benzyl groups, have on the rate of removal of halogen from compounds which may be grouped into

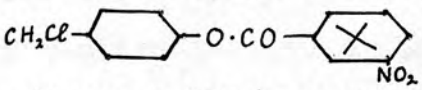
two sections (A) the isomeric ω-chloro-p-tolylnitro-benzoates and (B) the isomeric ω-chloro-p-tolylbromo-benzylethers. The formulae of these compounds are as follows.

(A)

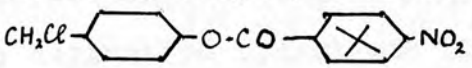
(a) ω-chloro-p-tolyl-o-nitrobenzoate



(b) ω-chloro-p-tolyl-m-nitrobenzoate

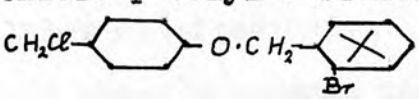


(c) ω-chloro-p-tolyl-p-nitrobenzoate

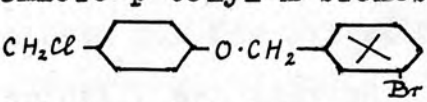


(B)

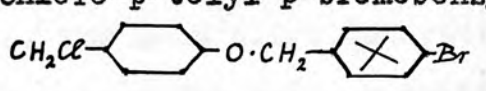
(a') ω-chloro-p-tolyl-o-bromobenzylether



(b') ω-chloro-p-tolyl-m-bromobenzylether.



(c') ω-chloro-p-tolyl-p-bromobenzylether.



The hydrolysis of these derivatives was carried out under the same conditions as were the corresponding unsubstituted compounds, i.e. the compounds not containing Br or NO_2 and the order of hydrolysis was found to be:-

In group (A) o < m < p < unsub. Graph II p. 15.

" " (B) o < m < p < unsub. Graph III p. 16.

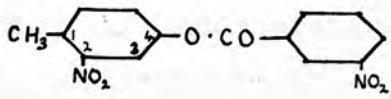
(o,m, and p- indicate the position of the NO_2 group in nuclei X in (A) and that of the Br group in (B).). The nitro group and bromine have a marked effect on

the reaction. The value of R_t was found to be as follows:-

(A) $R_{76°}$ (a) = 0.108, (b) = 0.160, (c) = 0.286

(B) $R_{25°}$ (a') = 0.370, (b') = 0.424, (c') = 0.833

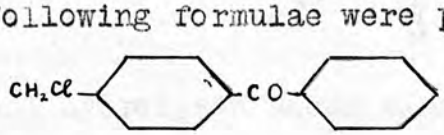
From a comparison of the values of R_t for the isomeric ω-chloro-p-tolylnitrobenzoates and that of $\omega - \omega'$-dichloro-di-p-tolylcarbonate it would be expected that the nitration of p-tolyl-o- and m-nitrobenzoates would give rise to 2-nitro-p-tolyl o- and m-nitrobenzoates whilst the nitration of the p-tolyl-p-nitrobenzoate, whose chloro derivative hydrolyses more rapidly than $\omega - \omega'$ dichloro-di-p-tolyl carbonate, would yield 3-nitro-p-tolyl-p-nitrobenzoate. Attempts were made to nitrate these compounds under the same conditions as those used for the nitration of di-p-tolyl-carbonate (loc.cit.) but they only proved successful in the case of the meta nitro derivative, the ortho and para nitro compounds being hydrolysed (see, nitration of p-tolylbenzoate p. 58.). The nitration of p-tolyl-m-nitrobenzoate, however, gave rise to a compound which was identified as 2-nitro-p-tolyl-m-nitrobenzoate of formula:-

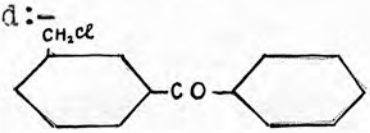


that is, the nitro group had entered the 2 position which is in agreement with the rate of hydrolysis obtained above.

The slow hydrolysis of the ω-bromotoluic

acids, as has already been pointed out, is due to the general polar effect (electron attracting and therefore deactivating effect) of the carbonyl group (>C=O) present in the carboxylic acid radical (— C(=O)OH).
The effect of this carbonyl group, acting through an oxygen atom, on the rate of removal of halogen, has been investigated in the case of ω -ω'-dichloro-di-p-tolylcarbonate and ω -chloro-p-tolyl benzoate (q.v.p.6).
The effect of the group when <u>directly</u> attached to the benzene nucleus was examined and for this purpose ω -chloro-m- and p-tolylphenylketones, with the following formulae were prepared:-

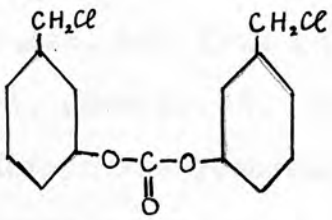




For comparative purposes these compounds were hydrolysed under the same conditions as those used for ω -ω' -dichloro-di-p-tolylcarbonate (q.v.p.50), but the rate of removal of halogen was found to be very slow and little difference could be detected between the rates of reaction of the two isomers (see Graph IV. p.17). The non-reactivity of this compound compared with that of the carbonate, is to be expected, because of the absence of any accelerating effect due to a hydroxyl group.

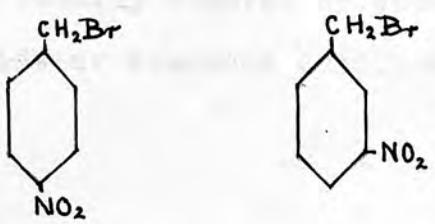
Since the hydrolysis of the compounds was too slow in 10% aqueous ethyl alcohol at 76°C the hydrolyses were carried out in 20% aqueous n-propyl alcohol at 100°C. In this way it was possible to

differentiate between the rate of removal of the halogen from the two compounds (see Graph V, p. 18.). The order of hydrolysis was found to be m>p which is in agreement with the results obtained from the ω-bromotoluic acids. This is the reverse of the order to be expected in the case of $\omega - \omega'$-dichloro-di-p and m-tolylcarbonates and in order to verify this $\omega - \omega'$ dichloro-di-m-tolylcarbonate of the following formula was prepared:-



and hydrolysed under similar conditions to those employed for the hydrolysis of the para-derivative (q.v.p. 50.). The order of hydrolysis was found to be p>m. For comparative purposes the hydrolysis curves of these compounds are given on pp 17 and 14, graph IV and I).

All the hydrolyses discussed hitherto were carried out in neutral to acid solution, that is, aqueous alcohol, as it has been observed that in certain cases the use of alkaline hydrolysing agents produces abnormal results .(cf. Ann.Reports Chem.Soc.1927,p.157). Measurements were made of the rate of hydrolysis, in alkaline solution, of meta and p-nitrobenzylbromides of formulae:-

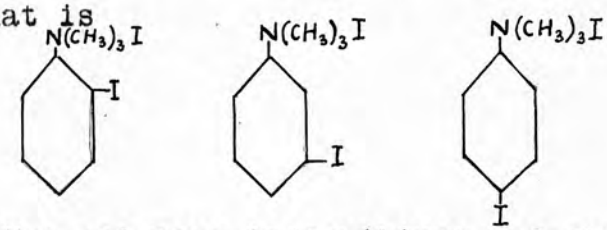


The progress of this reaction was observed by estimating the amount of acid formed at definite intervals of time and also by estimating the amount of bromidion liberated (by method of Volhard). Two experiments were performed using N/50 NaOH and N/10 NaOH at 25°C. In the case of the N/50 NaOH two regular curves were obtained but it was found that the order was $p > m$, the reverse of that estimated in acid solution (J.,1924, 125 1312). In the case of N/10 NaOH the reaction was greatly accelerated, but from an indirect estimation of acid produced, (See pp.19, Graph VI) more than 100% acid production was recorded. In both cases the percentage of bromine liberated was never greater than 100% and it was concluded that with NaOH a secondary reaction must have taken place.

Similar experiments were carried out with the ω-bromotoluic acids using N/20,N/100,N/250, N/500 NaOH as hydrolysing agent. In this case no abnormality was observed but it was found that the reaction was accelerated with dilution of alkali (See graph VII p. 20).

In recent work (Shoesmith and Slater,J.C.S., 1924,125 ; Nicollet and collaborators,J.A.C.S.,1927, 49 2, 1810), it has been shown that iodine atoms attached to those positions in a substituted benzene nucleus which are attacked with nitric acid, sulphuric acid etc., are readily removed by reducing agents such as hydrogen iodide or stannous chloride in hydrochloric

acid solution. The lability of the iodine is in some measure due to the same influences as those which govern substitution in the aromatic nucleus. It was therefore considered probable that different effects would be observed in iodo-derivatives of aniline which had been converted to compounds containing a group which did not allow activating electrons to pass down into the benzene nucleus and render the ortho and para positions capable of being attacked as they are in the case of the reduction of o- and p-iodoanilines and the corresponding phenomenon of substitution in the o- and p-position of the aniline nucleus. The compounds prepared for this purpose were the isomeric iodoanilines, the isomeric iododimethylanilines and the isomeric iodophenyltrimethylammonium iodides, that is

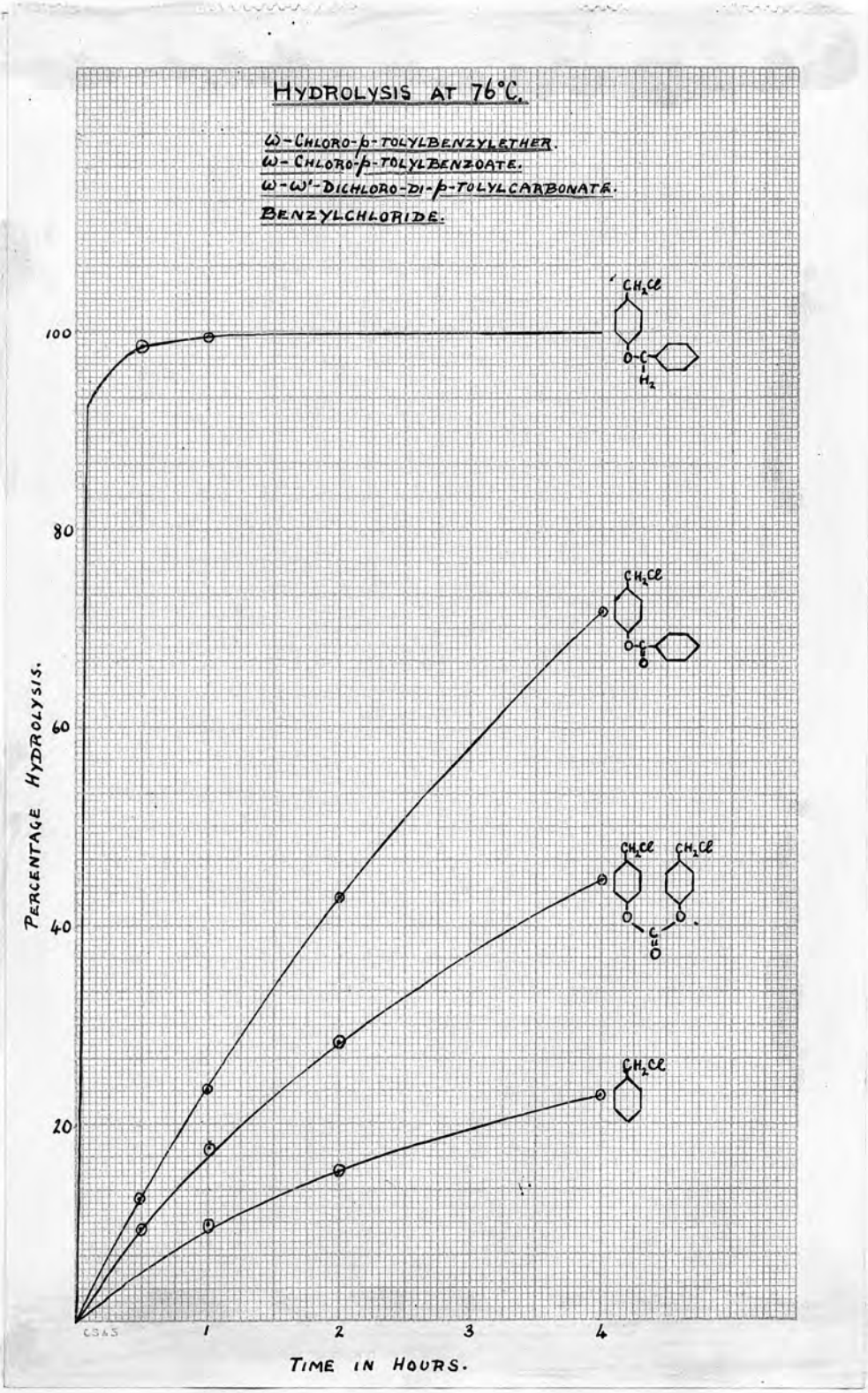


From the ortho and para-iodoanilines and also the corresponding iododimethyl anilines the iodine was readily removed by $SnCl_2$ and HCl in order o > p in the two cases Graph VIII, p. 21. The m-derivative was quite stable.

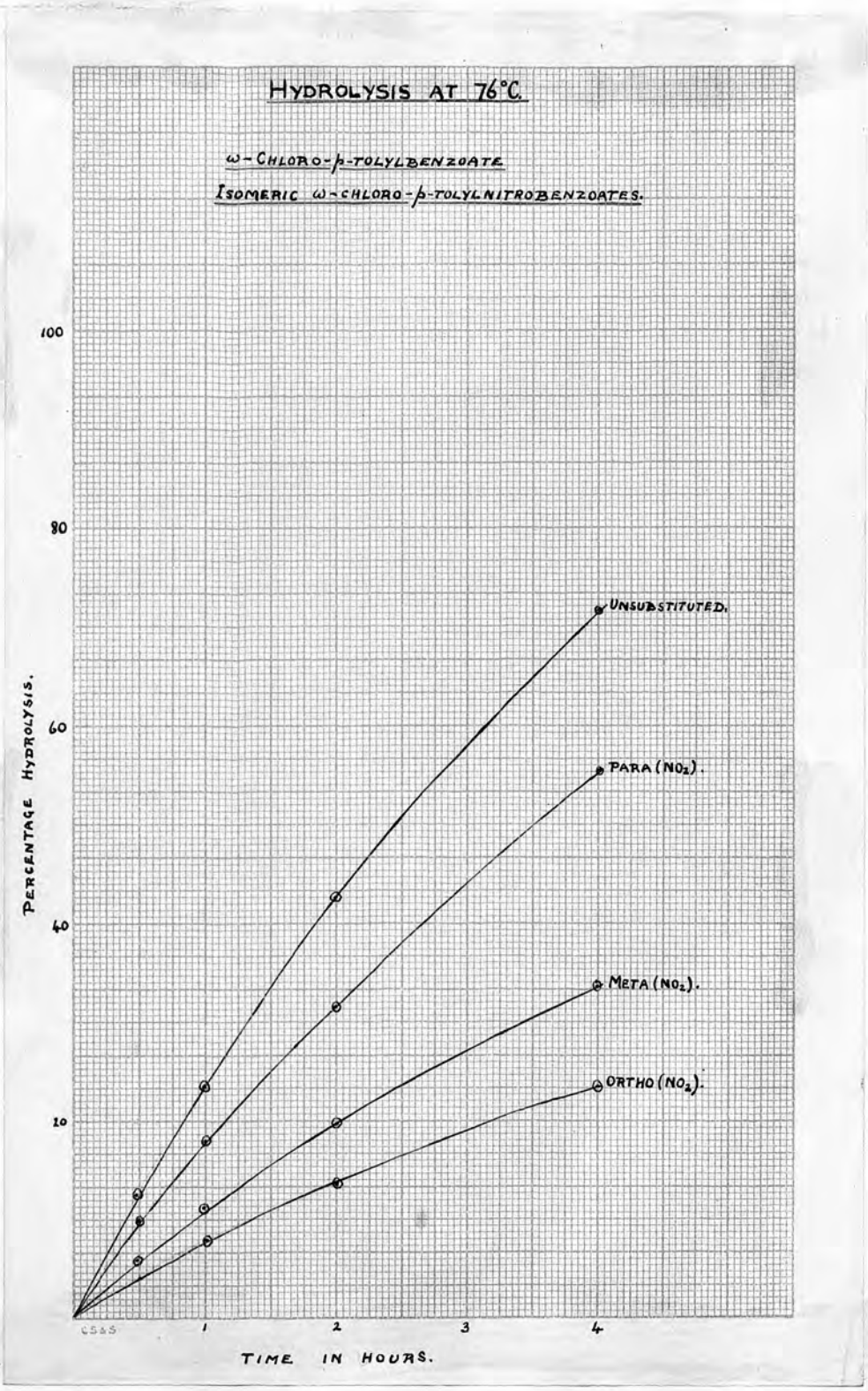
From the isomeric iodophenyltrimethylammonium iodides there was an immediate liberation of one atom of iodine, which was found to come, not from the nucleus, but from the side chain. This was proved to be the case since the m and p-iodophenyltrimethyl

ammoniumchlorides were prepared and subjected to the action of the reducing agent, when it was found that no iodine was liberated. The absence of reactivity in these quaternary salts and the results of all the experiments described are discussed on pp. 59,et seq.

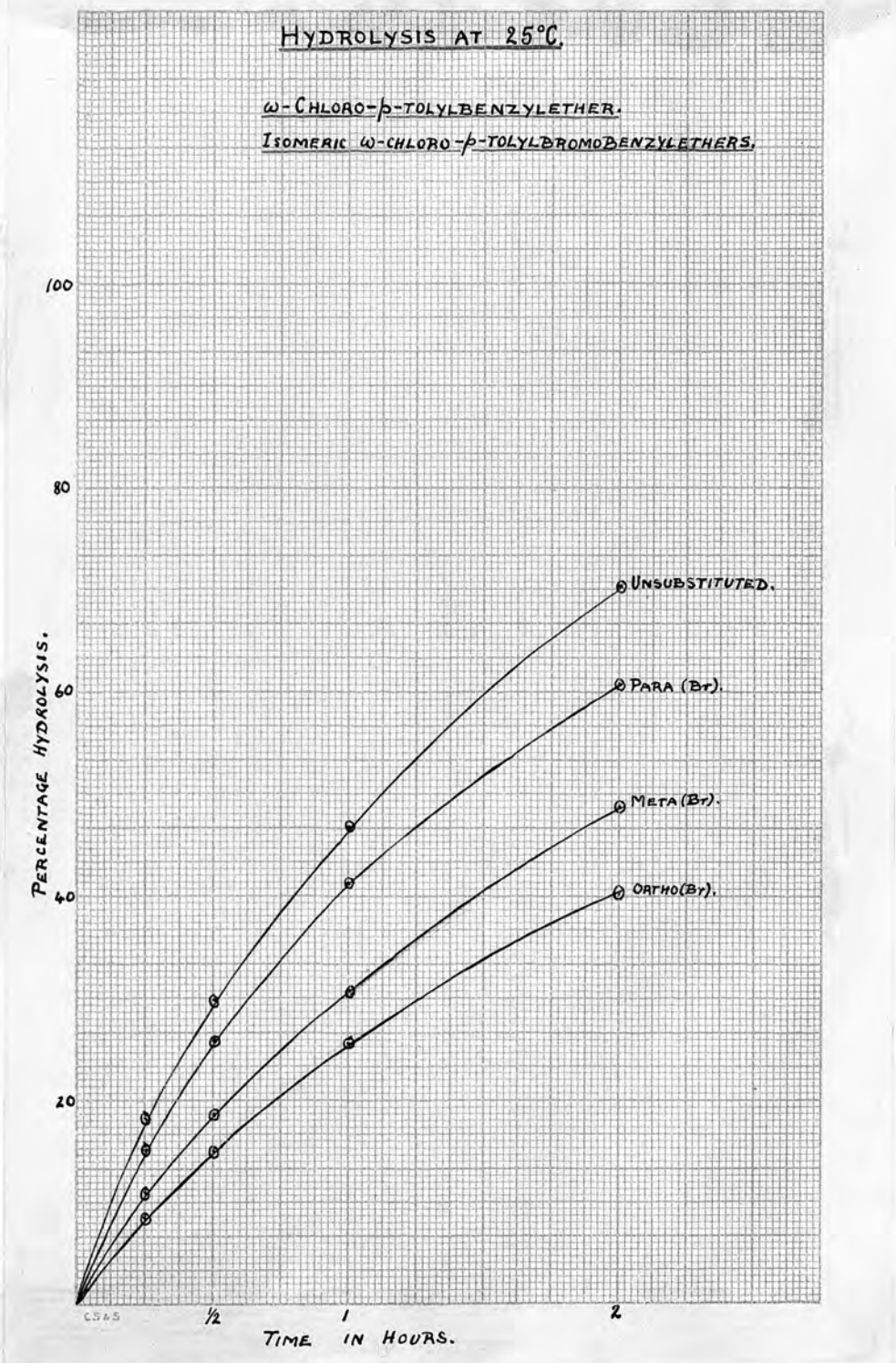
Graph I.


HYDROLYSIS AT 76°C.
ω-CHLORO-β-TOLYLBENZYLETHER.
ω-CHLORO-β-TOLYLBENZOATE.
ω-ω'-DICHLORO-DI-β-TOLYLCARBONATE.
BENZYLCHLORIDE.
PERCENTAGE HYDROLYSIS.
100
80
60
40
20
1
2
3
4
TIME IN HOURS.
CH2Cl
O
C
H2
O
C
O

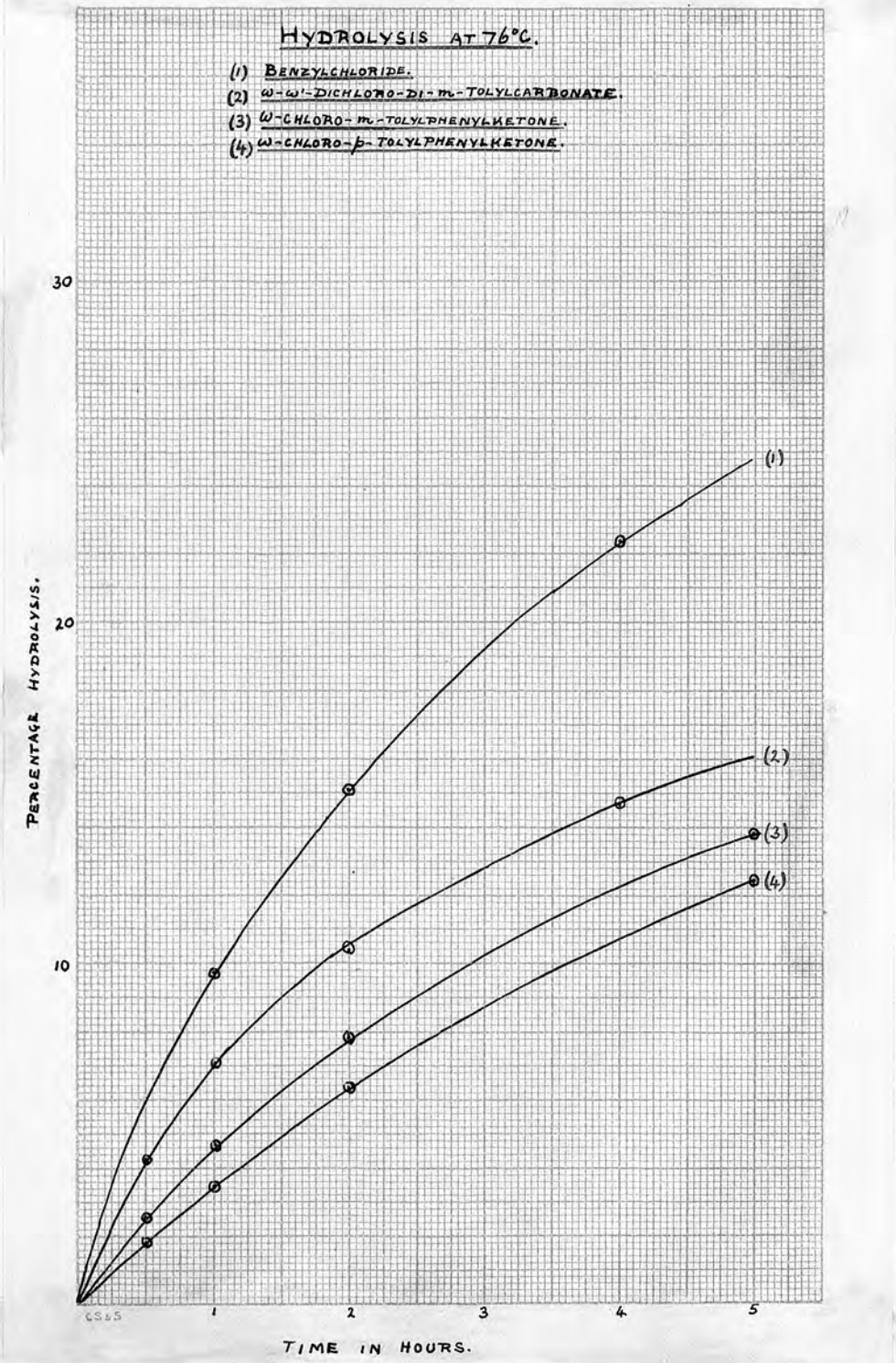
Graph II.


HYDROLYSIS AT 76°C.
ω-CHLORO-p-TOLYLBENZOATE
ISOMERIC ω-CHLORO-p-TOLYLNITROBENZOATES.
100
80
60
40
20
PERCENTAGE HYDROLYSIS.
UNSUBSTITUTED.
PARA (NO2).
META (NO2).
ORTHO (NO2).
1
2
3
4
TIME IN HOURS.

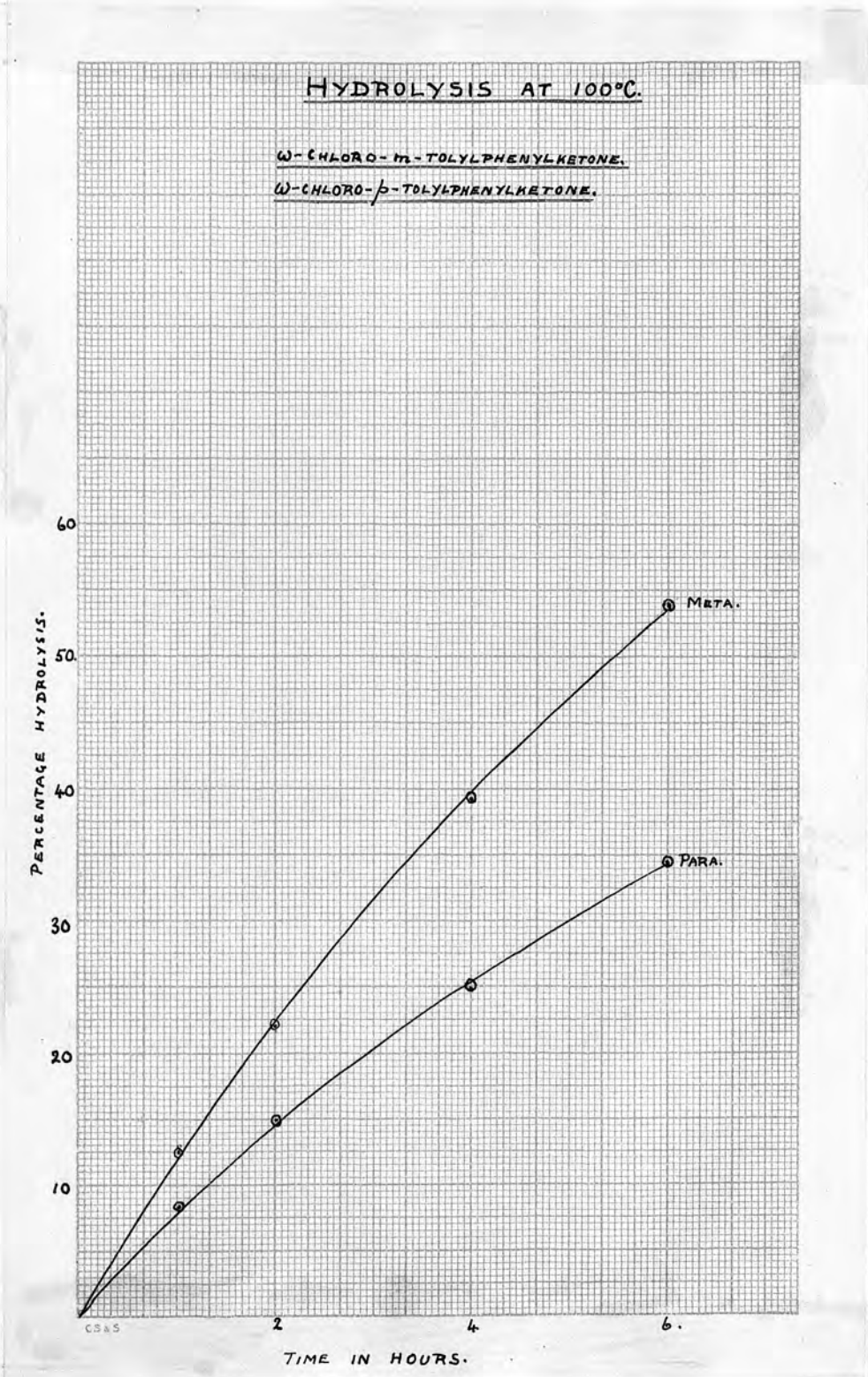
Graph III.


HYDROLYSIS AT 25°C.
ω-CHLORO-p-TOLYLBENZYLETHER.
ISOMERIC ω-CHLORO-p-TOLYLBROMOBENZYLETHERS.
100
80
60
40
20
PERCENTAGE HYDROLYSIS.
UNSUBSTITUTED.
PARA (Br).
META (Br).
ORTHO (Br).
½
1
2
TIME IN HOURS.

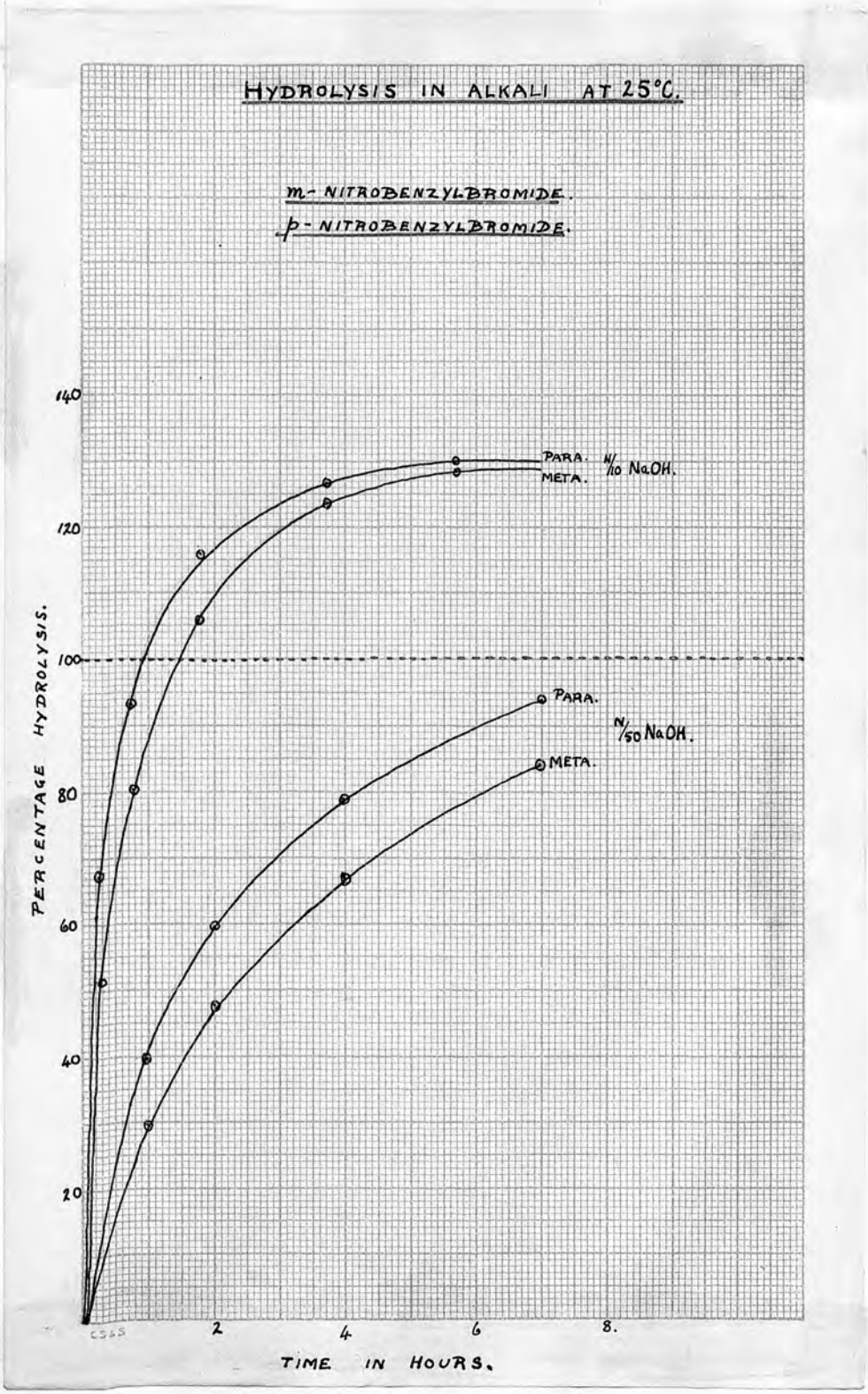
Graph IV.


HYDROLYSIS AT 76°C.
(1) BENZYLCHLORIDE.
(2) ω-ω'-DICHLORO-DI-m-TOLYLCARBONATE.
(3) ω-CHLORO-m-TOLYLPHENYLKETONE.
(4) ω-CHLORO-p-TOLYLPHENYLKETONE.
PERCENTAGE HYDROLYSIS.
30
20
10
(1)
(2)
(3)
(4)
1
2
3
4
5
TIME IN HOURS.

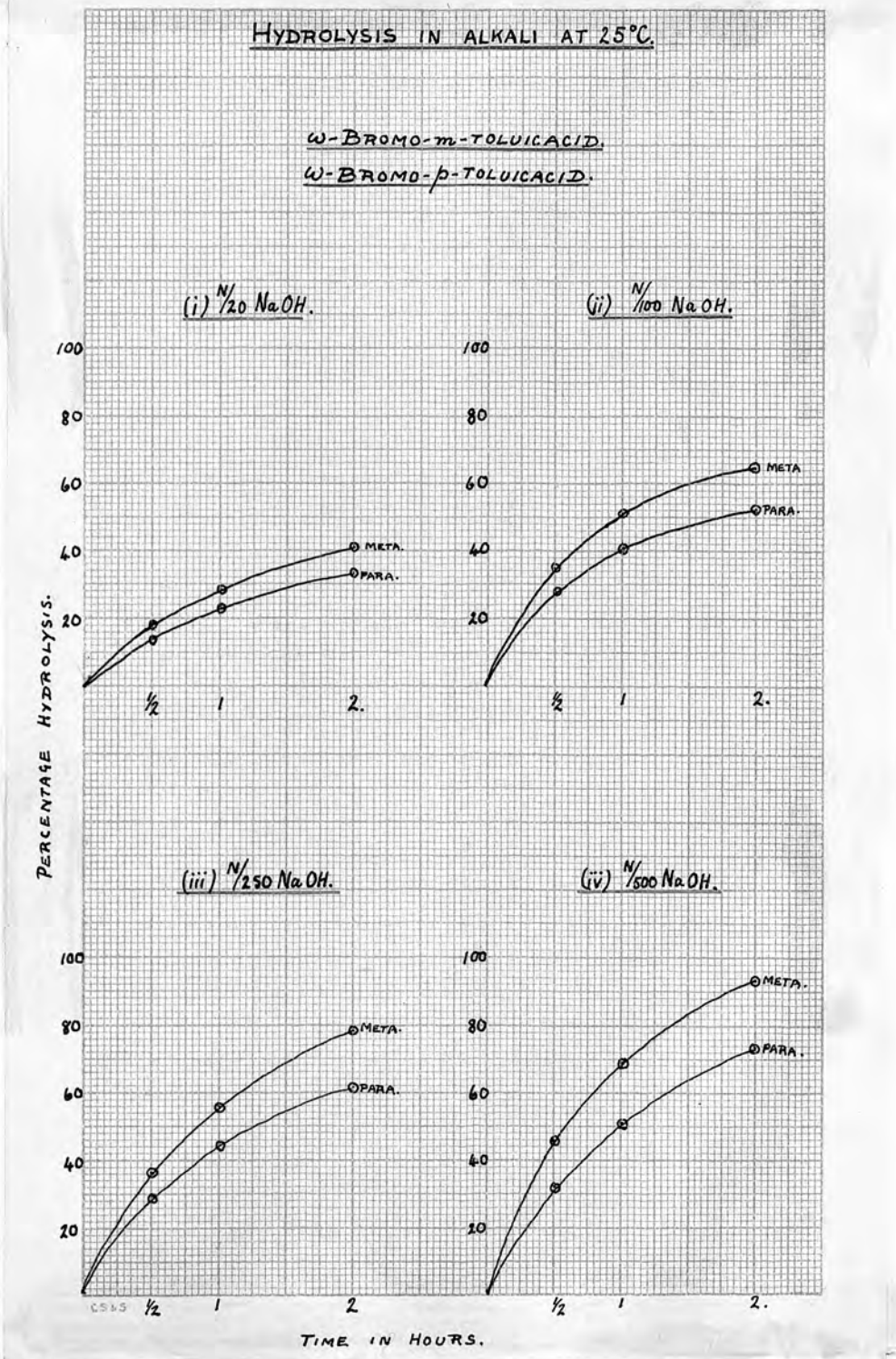
Graph V.


HYDROLYSIS AT 100°C.
ω-CHLORO-m-TOLYLPHENYLKETONE.
ω-CHLORO-p-TOLYLPHENYLKETONE.
PERCENTAGE HYDROLYSIS.
60
50
40
30
20
10
META.
PARA.
2
4
6.
TIME IN HOURS.
CS&S

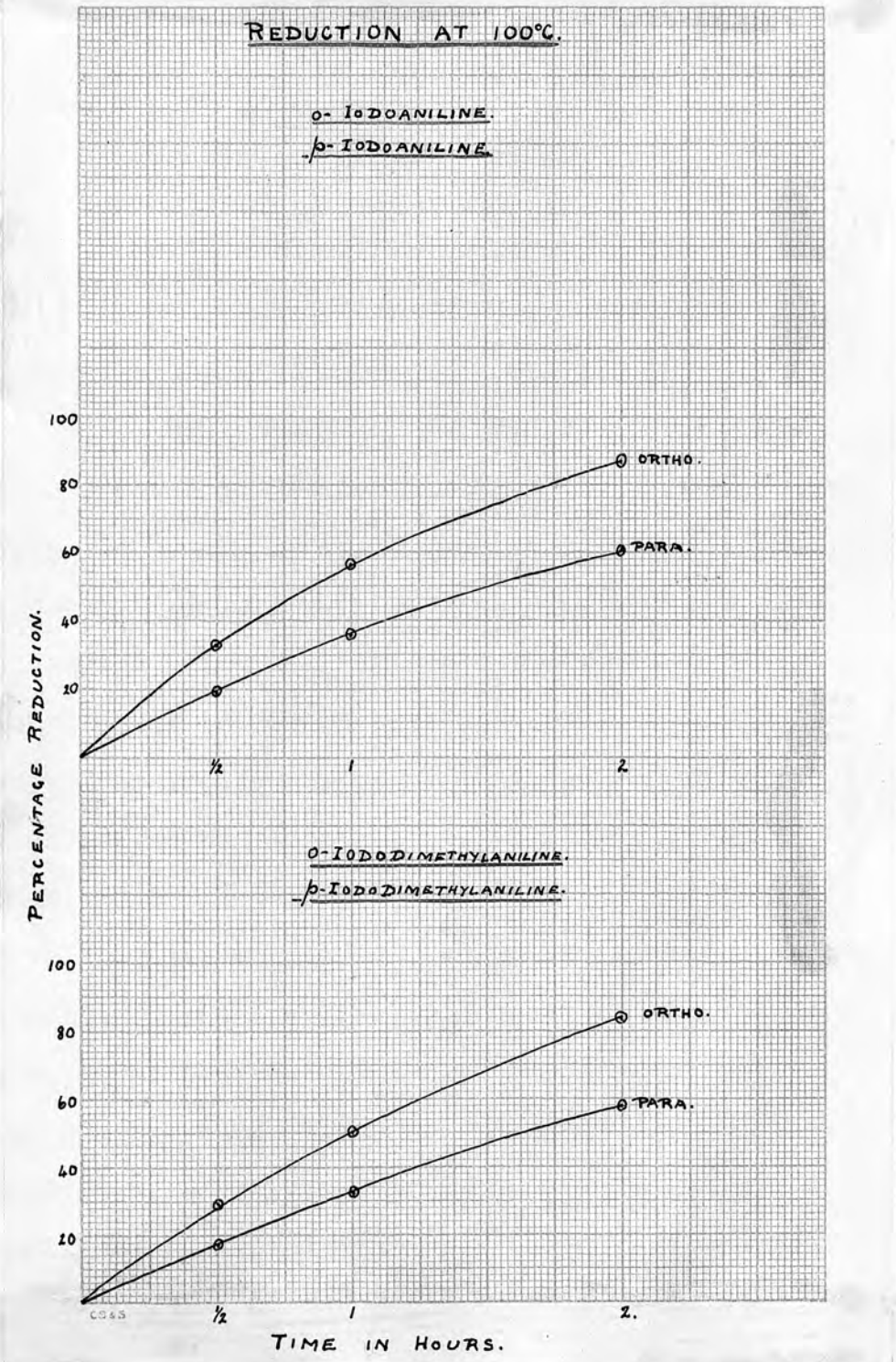
Graph VI.


HYDROLYSIS IN ALKALI AT 25°C.
m-NITROBENZYLBROMIDE.
p-NITROBENZYLBROMIDE.
PERCENTAGE HYDROLYSIS.
140
120
100
80
60
40
20
PARA.
META.
N/10 NaOH.
PARA.
META.
N/50 NaOH.
2
4
6
8.
TIME IN HOURS.

Graph VII.


HYDROLYSIS IN ALKALI AT 25°C.
ω-BROMO-m-TOLUICACID.
ω-BROMO-p-TOLUICACID.
(i) N/20 NaOH.
(ii) N/100 NaOH.
(iii) N/250 NaOH.
(iv) N/500 NaOH.
META.
PARA.
100
80
60
40
20
½
1
2.
PERCENTAGE HYDROLYSIS.
TIME IN HOURS.

Graph VIII.


REDUCTION AT 100°C.
o- IODOANILINE.
p- IODOANILINE.
100
80
60
40
20
ORTHO.
PARA.
½
1
2
PERCENTAGE REDUCTION.
o-IODODIMETHYLANILINE.
p-IODODIMETHYLANILINE.
100
80
60
40
20
ORTHO.
PARA.
½
1
2.
TIME IN HOURS.

PREPARATIVE.

ω-Chloro-p-tolylbenzoate.

This compound was prepared by a method summarised as follows:-

$$CH_3.C_6H_4OH + ClOC.C_6H_5 \xrightarrow{KOH} CH_3.C_6H_4.O.CO.C_6H_5$$

$$\xrightarrow{Cl_2,\ 180\text{-}200^\circ C} CH_2Cl.C_6H_4.O.CO.C_6H_5.$$

p-Tolylbenzoate. (Guareschi, Annalen, 1871, 171, 142).

This compound was not made according to the method given in the above reference as it was readily prepared by the Schotten-Baumann reaction. p-Cresol (50 gms.) emulsified with 50 c.c. water in a litre flask was mixed with 65 gms. benzoylchloride and a solution of potassium hydroxide added with shaking until the liquid remained alkaline. The whole was then warmed on the steam-bath for half an hour with continuous agitation. On cooling p-tolylbenzoate crystallised out and was recrystallised from aqueous alcohol from which it separated in white prismatic needles of melting point 71°C. (Guareschi 71.5°C).

ω-Chloro-p-tolylbenzoate was prepared by the direct chlorination of p-tolylbenzoate at 180-200°C. p-Tolylbenzoate (25 gms.) was placed in a weighed 100 c.c. flask fitted with a stirrer, inlet tube and condenser. The flask was immersed in an oil bath whose temperature was maintained at 180° to 200°C.

throughout the experiment. Chlorine gas, dried by passage through two wash bottles containing concentrated H_2SO_4 was bubbled through the vigorously stirred liquid in the flask until an increase in weight of 4.1 gms. was obtained. This increase in weight of the p-tolylbenzoate corresponded to the weight of chlorine required to form its monochloro derivative and was observed by weighing the flask after intervals of half an hour and one hour. When the required increase in weight had taken place (one and a half hours were required) the contents of the flask were allowed to cool slowly. The chlorination product was a brown viscous oil which solidified after a period of 48 hours when it was pressed on a porous plate, crystallised from light petroleum (b.p. 60-80°C.) and finally from n-propyl alcohol from which it separated in white rectangular plates of melting point 112-113°C.

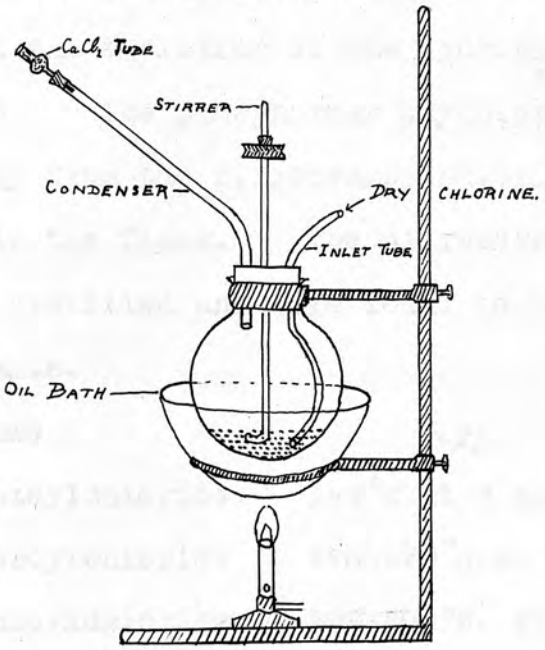
This compound was found to contain 14.30% hydrolysable chlorine ($C_{14}H_{11}O_2Cl$ requires 14.40% hydrolysable chlorine).

Note. Estimation of Hydrolysable Chlorine by method of Volhard.

The percentage of hydrolysable chlorine was estimated by heating a weighed quantity (0.2 gm.) of the substance with 10 c.c. of 10% alcoholic KOH for 30 minutes on the steam-bath, when it was cooled, diluted with distilled water and acidified with 5 c.c.

of concentrated HNO_3. Twenty c.c. of N/20 $AgNO_3$ were now added and the excess of $AgNO_3$ was titrated with N/20 NH_4CNS using ferric alum as indicator.

The above method of chlorination proved so successful that it was used in subsequent direct chlorination experiments. The apparatus used for all direct chlorination preparations is illustrated below.



Preparation of the isomeric ω -chloro-p-tolylnitrobenzoates.

These compounds were prepared by reactions summarised as follows:-

$$NO_2.C_6H_4.COOH + PCl_5 \longrightarrow NO_2.C_6H_4.COCl + POCl_3 + HCl$$

$$NO_2.C_6H_4.COCl + HO.C_6H_4.CH_3 \xrightarrow{KOH} NO_2.C_6H_4.CO.O.C_6H_4.CH_3$$

$$NO_2.C_6H_4.CO.O.C_6H_4.CH_3 \xrightarrow[Cl_2\ 180\text{-}200^\circ C.]{} NO_2.C_6H_4.CO.O.C_6H_4.CH_2Cl.$$

Isomeric nitrobenzoylchlorides (Adams, Organic Syntheses 1923, 3, 75) (Claisen, Shadwell, Ber., 1879, 12, 351, 1943). Phosphorus pentachloride (65 gms.) was added to o-, m- and p-nitrobenzoic acids (50 gms.) in a 500 c.c. distilling flask fitted with a reflux condenser and having its side tube closed. The mixture was well shaken and heated on the steam-bath until completely liquid and the evolution of the hydrochloric acid gas had ceased. The phosphorous oxychloride was distilled away from the nitrobenzoylchloride which remained in the flask. The nitrobenzoylchlorides were each distilled and were found to have the following constants.

Name.	b.p.	m.p.
o-nitrobenzoylchloride	148°C at 9 mm.	24-25°C.
m-nitrobenzoylchloride	275-278°C. at 760 mm.	35°C.
p-nitrobenzoylchloride	202-205°C. at 105 mm.	75°C.

Isomeric p-tolylnitrobenzoates (Eugen Hanggi, Helv. Chim. Acta, 4 25) p-Cresol (34 gms.) was added to the nitrobenzoylchloride (50 gms.), and KOH solution run in with shaking and warming until the solution was strongly alkaline. On cooling a white solid crystallised out which was filtered off, washed with water and recrystallised from aqueous alcohol. The p-tolylnitrobenzoates are all white crystalline solids with the following melting points and crystalline forms:-

Name	m.p.	Solvent and crystalline form.
p-tolyl-o-nitrobenzoate.	98-98.5°C.	tables from alcohol
p-tolyl-m-nitrobenzoate	77-78°C.	needles from alcohol
p-tolyl-p-nitrobenzoate	78-79°C.	needles from alcohol.

Isomeric ω-chloro-p-tolylnitrobenzoates.

The p-tolylnitrobenzoates were chlorinated in the same way as p-tolylbenzoate (q.v.p. 22). In each case dry chlorine gas was passed into the p-tolylnitrobenzoate (25 gms.) until an increase in weight of 3.4 gms. was obtained. The chlorination product, when solid, was recrystallised first from absolute alcohol, then from light petroleum (b.p. 80-100°C.) from which the ω-chloro-p-tolylnitrobenzoates crystallised in white rectangular plates. The m.p.'s and hydrolysable chlorine content of these compounds were as below:-

Name.	m.p.	Cl found	Cl reqd.
ω-chloro-p-tolyl o-nitrobenzoate.	96-97°C	12.20%	12.17%
ω-chloro-p-tolyl m-nitrobenzoate.	85-86°C	12.10%	12.17%
ω-chloro-p-tolyl p-nitrobenzoate.	114.5 - 115.5°C	12.00%	12.17%

Preparation of ω-chloro-p-tolylbenzylether.

An attempt was made to prepare this compound by an analogous method to that employed for the preparation of ω-chloro-p-tolylbenzoate. It was not found possible to prepare ω-chloro-p-tolylbenzylether in this way because chlorine entered the nucleus of

p-tolylbenzylether and not the side chain.

The reactions employed are summarised as follows:-

$$CH_3.C_6H_4.OH + ClCH_2.C_6H_5 \xrightarrow{KOH} CH_3.C_6H_4.O.CH_2C_6H_5$$

$$\swarrow Cl_2\ 180°\text{-}200°\ C.$$

$$CH_3.C_6H_3Cl.O.CH_2C_6H_5 \text{ (probably).}$$

p-Tolylbenzylether (Staedel, Annalen 1883, 217, 44)

Potassium hydroxide (28 gms. was dissolved in 25 c.c. water and the solution made up to 60 c.c. with absolute alcohol. This solution was added to 50 gms. p-cresol in a 500 c.c. flask fitted with a relfux condenser. The solution was heated on the steam bath, 50 gms. benzylchloride slowly added and the mixture briskly agitated. As the reaction proceeded KCl was precipitated and the reaction was complete when this precipitation ended. The alcohol was than distilled away and the residue in the flask shaken up with warm KOH solution to neutralise any excess benzylchloride. The reaction mixture was cooled when the white p-tolylbenzylether separated out. This was filtered off, washed with water and recrystallised from aqueous alcohol from which it separated in hexagonal plates of m.p. 41° C.

Chlorination of p-tolylbenzylether.

p-Tolylbenzylether (25 gms.) was chlorinated in the same way as was p-tolylbenzoate (q.v.p. 22). An increase in weight of 4.2 gms. was obtained which corresponds to a monochloroderivative of p-tolylbenzyl-

ether. The chlorination product, in this case, would not solidify and decomposed with production of tar when an attempt was made to distil it under reduced pressure. Several chlorinations were performed with the same result. Finally air was drawn through a crude chlorination product in order to remove traces of chlorine and hydrogen chloride. The hydrolysable chlorine content of a sample of this oil was estimated. It contained 2% : $C_{14}H_{13}OCl$ requires 15.2%. An estimation of the total chlorine content by Carius' method was carried out. Found: 14.5% ($C_{14}H_{13}OCl$) required 15.2%. It was therefore evident that the direct chlorination of p-tolylbenzyl-ether results in nuclear chlorinated products. This shows the strong nuclear directing influence exerted by the oxygen atom in the molecule (cf. Shoesmith and Connor J.C.S., 1927, 2230).

A second method was employed for the preparation of ω-chloro-p-tolylbenzylether which proved successful and is summarised in the following reactions.

$$CHO.C_6H_4OH + Cl.CH_2.C_6H_5 \xrightarrow[\text{alcohol}]{KOH} CHO.C_6H_4.O.CH_2C_6H_5.$$

$$CH_2OH.C_6H_4.O.CH_2.C_6H_5. \xrightarrow{25\% \text{ Alcoholic KOH}} CH_2Cl.C_6H_4.O.CH_2C_6H_5. \xleftarrow[\text{Benzene}]{HCl \text{ gas}}$$

p-Benzyloxybenzaldehyde. (Emil Worner, Ber., 1897, 29 139-160).

A slight modification of Worner's method had to be made in this preparation since it was found that better yields were obtained when ethyl alcoholic

KOH was used instead of aqueous KOH. Potassium hydroxide (11.5 gms.) was dissolved in 10 c.c. water and the solution made up to 50 c.c. with absolute alcohol. This solution was added to 25 gms. p-hydroxybenzaldehyde in a 250 c.c. flask fitted with a reflux condenser. The solution was warmed on the steam bath until the p-hydroxybenzaldehyde passed into solution when 25 gms. benzylchloride were added, the reaction mixture being agitated. The p-benzyloxybenzaldehyde was isolated in the same way as p-tolylbenzylether (q.v.p. 27.). It was finally recrystallised from light petroleum (b.p. 40-60°C) from which it separated in pale yellow needles of melting point 73°C.

Yield 60% of that expected.

p-Benzyloxybenzylalcohol.

This compound was prepared from p-benzyloxybenzaldehyde by means of Cannizzaro's reaction. p-Benzyloxybenzaldehyde (20 gms.) was dissolved in 60 c.c. of 25% ethylalcoholic KOH. The solution was warmed on the steam-bath for half an hour, after which crystals of the sodium salt of p-benzyloxybenzoic acid began to separate. The contents of the flask were allowed to stand for 24 hours when they became completely solid. Water was added and the solution extracted with ether. The ethereal solution was extracted twice with aqueous NaOH in order to remove all the acid formed in the reaction and finally with water. The ether layer was dried over anhydrous sodium sulphate

and the ether evaporated away from the p-benzyloxy-benzylalcohol which solidified on cooling and was recrystallised from light petroleum (b.p. 60-80°C.) from which it separated in rectangular plates of melting point 78°C. An analysis of this compound resulted as follows:- Found C, 78.3; H,6.4. $C_{14}H_{14}O_2$ requires C,78.50; H,6.54%.

The alkaline layer obtained in the above preparation was acidified with dil.HCl when p-benzyloxybenzoic acid was precipitated. This acid was filtered and recrystallised from water from which it separated in white needles of melting point 189-190°C. (Cohen, Dudley,Chem.Zentr.,1910,2,1380 needles m.p. 189-190°C.).

ω-Chloro-p-tolylbenzylether.

p-Benzyloxybenzylalcohol (8 gms.) was dissolved in 20 c.c. benzene in a 100 c.c. flask fitted with an inlet tube and an outlet calcium chloride tube. This solution was saturated with dry hydrogen chloride. The water formed in the reaction was separated from the benzene layer which was dried over $CaCl_2$,the benzene evaporated away in vacuo and the solid residue was recrystallised from light petroleum (b.p. 40-60°C.) from which ω-chloro p-tolylbenzylether separated in pale yellow rectangular plates of melting point 74°C. This compound was found to contain 15.1% hydrolysable chlorine. $CH_2Cl.C_6H_4.O.CH_2C_6H_5$ requires 15.2% hydrolysable chlorine.

Isomeric ω-chloro-p-tolylbromobenzylethers.

These compounds were prepared by an analogous method to that employed for the preparation of ω-chloro-p-tolylbenzylether. The reactions are summarised as follows:-

$$CH_3C_6H_4Br + Br_2 \xrightarrow{180^\circ C.} CH_2Br.C_6H_4Br$$

$$CH_2.Br.C_6H_4.Br + OH.C_6H_4.CHO \xrightarrow[\text{alcohol}]{KOH} Br.C_6H_4.CH_2.O.C_6H_4CHO$$

$$Br.C_6H_4.CH_2.O.C_6H_4.CH_2OH. \xrightarrow{25\% \text{ alcoholic KOH.}} Br.C_6H_4.CH_2.O.C_6H_4.CH_2Cl \xleftarrow[\text{Benzene}]{HCl \text{ gas}}$$

Isomeric bromotoluenes.

o-Bromotoluene was redistilled and the fraction with b.p. 181-183°C. collected. The para isomeride was purified similarly and had a b.p. 181°C. m-Bromotoluene was prepared from m-toluidine by the Sandmeyer reaction as follows:- (Adams, Organic Syntheses, 1925, 5 21).

$$CH_3.C_6H_4.NH_2 + HNO_2 + H_2SO_4 \longrightarrow CH_3.C_6H_4.N_2SO_4H.$$

$$CH_3.C_6H_4.N_2SO_4H + HBr\ (+CuBr) \longrightarrow CH_3.C_6H_4Br.$$

The Sandmeyer reagent, HBr-CuBr solution, was first prepared and the diazonium solution was added slowly to it. A current of steam was simultaneously passed through the heated solution. The m-bromotoluene resulting from this steam-distillation was extracted, purified and distilled at 183°C. The yield was 50% of that expected.

Isomeric bromobenzylbromides (Shoesmith and Slater, J.C.S., 1926,218). These compounds were prepared by the direct bromination of the boiling bromotoluenes. The requisite bromotoluene (30 gms.) was heated to boiling in a 100 c.c. flask and 9.5 c.c. bromine were passed into the liquid in the form of vapour. This addition took place over a period of three hours. The reaction products were distilled under reduced pressure and the fraction boiling between 120°and 130°C at 14 mm. collected. The resulting bromobenzyl bromides crystallised on cooling and were employed for the next preparation without further purification.

Isomeric bromobenzyloxybenzaldehydes.

p-Hydroxybenzaldehyde (12.5 gms.), dissolved in a solution of 6 gms. KOH in 6 c.c. water and 20 c.c. absolute alcohol, was added to the requisite bromobenzylbromide (25 gms.) dissolved in 30 c.c. absolute alcohol in a 100 c.c. flask fitted with a reflux condenser. This was boiled on the steam bath for two hours, poured into an excess of water and the resulting bromobenzyloxy-benzaldehydes purified in the same way as was p-benzyl-oxybenzaldehyde (q.v.p. 28.). The bromine content, m.p. and crystalline form of these new aldehydes was found to be as follows-

Name	m.p.	Cryst. Form	Solvent	Br found
o-bromobenzyloxybenzaldehyde.	53-54°C.	Rect. Plates	Alcohol	27.40%
m-bromobenzyloxybenzaldehyde.	67-68°C.	Prismatic needles	Alcohol	27.60%
p-bromobenzyloxybenzaldehyde.	86-87°C.	Rect, Prisms	Alcohol	27.66%

($C_{14}H_{11}O_2Br$ requires Br 27.46%)

Isomeric bromobenzyloxybenzaldehydephenylhydrazones.

These compounds were prepared by the action of phenylhydrazine on a solution of the requisite aldehyde in glacial acetic acid. The ortho and meta derivatives were recrystallised from hot alcohol but the para derivative was sparingly soluble in this solvent and had to be recrystallised from acetone.

The bromine content, crystalline form and melting point of these new phenylhydrazones was found to be as under.

Name.	M.p.	Crys. Form	%Br found
o-bromobenzyloxybenzaldehyde-phenylhydrazone.	135.5-136°C	Rhombic Plates	20.70
m-bromobenzyloxybenzaldehyde-phenylhydrazone.	129-130°C.	Rect. Plates	20.81
p-bromobenzyloxybenzaldehyde-phenylhydrazone.	151-152°C.	Rect. Plates	20.75

($C_{20}H_{18}O N_2$ requires Br; 20.98%)

Note.

Estimation of halogen by the method of catalytic hydrogenation. (Ter Meulen, Organ. Chem. Analysis, Thorpe and Whitely 1926, 275). Fifty milligrams of the halogen compound were weighed accurately in a procelain boat. The boat was then placed in one end of a combustion tube (100 cm. long x 1 cm. in diam.) through which a slow stream of hydrogen and ammonia was passed. The middle part of the tube was heated to dull redness and as the contents of the boat were gradually heated with a small flame the ammonium halide was deposited at the cool end of the tube. When all the substance in the boat had been decomposed the tube was allowed

to cool, the ammonium halide washed out with distilled water and the halogen in this solution estimated by method of Volhard.(q.v.p. 23).

Isomeric bromobenzyloxybenzylalcohols.

These compounds were prepared from the corresponding aldehydes by Cannizzaro's reaction and were isolated and purified by a method analogous to that employed for the preparation of p-benzyloxybenzyl-alcohol (q.v.p.29). It was found necessary in this case to remove impurity formed in the reduction by boiling up an alcoholic solution of the alcohols with animal charcoal. The bromobenzyloxybenzylalcohols were finally recrystallised from absolute alcohol from which the ortho derivative separated in white prismatic needles of m.p. 99-100°C; Found: Br 26.95%, the meta derivative in Rect.Plates of m.p. 79-80°C; Found: Br, 27.0% and the para derivative in rect.plates of m.p. 107-108°C; Found:Br, 27.30%.

($C_{14}H_{13}O_2Br$ requires Br, 27.27%)

Isomeric bromobenzyloxybenzoicacids.

These acids were precipitated from the alkaline layer obtained in the above preparation. An acetone solution of the acids was boiled up with animal charcoal in order to remove colouring matter and a small amount of tar formed in the reduction. The ortho acid was recrystallised from alcohol from which it separated in long needles of m.p. 197.5-198°C. Found Br 26.0%; the meta and para acids from acetone from which they

separated in rectangular plates. The meta acid had m.p. of 205.5-206°C. Found Br 26.38%; and the para acid had m.p. of 228-230°C. Found Br 25.80%.

($C_{14}H_{11}O_3Br$ requires Br 26.03%).

Isomeric ω-chloro-p-tolylbromobenzylethers.

These compounds were prepared from the corresponding alcohols by a method analogous to that employed for the preparation of ω-chloro-p-tolylbenzylether. (q.v.p. 30).

The ω-chloro-p-tolylbromobenzylethers were recrystallised from light petroleum (b.p. 60-80°C) from which they separated in rectangular prisms. The ortho derivative had m.p. 78.5-79°C; found Cl (hydrolysable) 11.30%, the meta derivative m.p. 68-69°C; found Cl (hydrolysable) 11.35% and the para derivative m.p. 88-89°C; found Cl (hydrolysable) 11.21%.

($C_{14}H_{12}OCl$ requires Cl (hydrolysable) 11.40%)

Preparation of ω-ω'-dichloro-di-p and m-tolylcarbonates.

These compounds were prepared by the direct chlorination of the corresponding tolylcarbonates at 180-200°C.

$$(CH_3C_6H_4O)_2\,CO + Cl_2 \xrightarrow{180°C} (CH_2Cl.C_6H_4O)_2\,CO + HCl$$

The method was the same as that employed for the chlorination of p-tolylbenzoate. In this case an increase in weight of 7.3 gms. was required for 25 gms. of tolylcarbonate.

ω - ω' Dichloro-di-p-tolylcarbonate.

The chlorination product of p-tolylcarbonate solidified with great difficulty and had to be allowed to stand on a porous plate for a long period before it could be finally purified. The ω - ω'-dichloro-di-p-tolylcarbonate was then recrystallised from light petroleum (b.p. 60-80°C) from which it separated in rectangular plates of m.p. 81-82°C. Found: Cl, (hydrolysable) 22.5 $C_{15}H_{12}O_3Cl_2$ requires Cl(hydrolysable) 22.8%.

ω - ω' -Dichloro-di-m-tolylcarbonate.

The chlorination product of m-tolylcarbonate would not solidify therefore the dark brown oil was distilled under reduced pressure. A clear viscous syrup of b.p. 135-140°C at 9 mm. was obtained. This fraction solidified after 48 hours and was recrystallised from absolute alcohol from which the ω - ω'-dichloro-di-m-tolylcarbonate separated in rectangular prisms of m.p. 59-60°C. Found: Cl (hydrolysable) 22.7 $C_{15}H_{12}O_3Cl_2$ requires Cl (hydrolysable) 22.8%.

ω -Bromo-m-and p-toluic acids. (Shoesmith and Hetherington, J.C.S., 1924,128,1314).

The reactions are summarised as follows:-

$$CH_3C_6H_4.COOH \xrightarrow{SOCl_2} CH_3.C_6H_4.COCl \xrightarrow{Br_2} CH_2Br.C_6H_4.CO\,Br \xrightarrow[98\%]{HCO_2H} CH_2Br.C_6H_4COOH.$$

m-and p-Toluoylchlorides.

The toluic acids were converted to the acid chlorides by heating 50 gms. of acid with a slight excess (45 gms.) thionyl chloride until no more hydrogen chloride was evolved. The m- and p-toluoylchlorides thus obtained were purified by distillation and had b.p's:- meta 84.5-86°C at 9 mm; para 100°C at 14 mm.

m- and p-ω -bromotoluoylbromides.(Davies and Perkin, J.C.S., 1922, 121 2202.).

Bromine (16.3 c.c.) was added slowly to the requisite toluoylchloride (49 gms.) maintained at 185-195°C so that the reaction was ended after one hour forty minutes. The resulting ω-bromo-toluoylbromides were purified by distillation under reduced pressure, and were colourless liquids which fumed on exposure to the atmosphere and decomposed rapidly with evolution of HBr. ω -Bromo-p-toluoylbromide had b.p. 175°C at 15 mm. and ω-bromo-m-toluoylbromide had b.p. 160-165°C at 14 mm. These compounds solidified on cooling.

ω-Bromo-m- and p-toluicacids.

The ω-bromotoluoylbromides were converted to the corresponding ω-bromotoluicacids by heating them with formic acid solution. The acid bromide was placed in a flask with 12 times its weight of 98-100% formic acid and warmed gently to a temperature of 30-35°C. The hydrolysis was complete after 1 hour and the product was obtained by pouring into an excess of water

when it was filtered off. The ω-bromotoluic acids were recrystallised several times from benzene from which they finally separated as white crystalline solids of m.p.'s:-ω-bromo-m-toluic acid 150°C; Found Br (hydrolysable) 37.41%; ω-bromo-p-toluicacid 223°C. Found Br (hydrolysable) 37.3%. $C_8H_7O_2Br$ requires Br (hydrolysable) 37.20%.

ω-Chloro-m- and p-tolylphenylketones.

The para derivative had already been prepared (Thorner, Annalen, 1877, 189 84) but the meta derivative had not been previously synthesised. Both compounds were prepared by the direct chlorination of the corresponding tolylphenylketone.

ω-Chloro-m-tolylphenylketone.

This compound was prepared by a method summarised as follows:-

$$CH_3.C_6H_4.COOH \xrightarrow{SOCl_2} CH_3.C_6H_4.COCl$$

$$CH_3.C_6H_4.COCl + C_6H_6 \xrightarrow{AlCl_3} CH_3.C_6H_4.CO.C_6H_5 \xrightarrow[120^\circ C]{Cl_2} CH_2Cl.C_6H_4.CO.C_6H_5$$

m-Tolylphenylketone. (Ador, Rilliet, Ber., 1879, 12, 2300).

m-Toluoyl chloride (22 gms.) (q.v.p. 32.) was added slowly to a mixture of 25 gms. $AlCl_3$ in 250 c.c. benzene. When all the toluoylchloride had been added the reaction mixture was heated to boiling until there was no further evolution of hydrogen chloride. The dark green liquid so obtained was poured into a large excess of water, the benzene layer separated off and washed twice with dilute NaOH. The benzene was then

evaporated away from the m-tolylphenylketone which was distilled under reduced pressure and had b.p.162°C. at 10 mm. The yield was 82% of that expected.

ω-Chloro-m-tolylphenylketone.

m-Tolylphenylketone (22.5 gms.) in a 100 c.c. flask was maintained at a temperature of 120°C. and dry chlorine was passed into the hot liquid until there was an increase in weight of 4.1 gms. The chlorination product was distilled under reduced pressure and the fraction with b.p. 190-196°C. at 10 mm. collected. This was a clear viscous oil which solidified completely after standing for twenty-four hours and this solid was recrystallised from light petroleum (b.p. 60-80°C.) from which the ω-chloro-m-tolylphenylketone separated in clear rhombic prisms of m.p. 47-48°C. Found: Cl(hydrolysable) 15.17% $C_{14}H_{11}OCl$ requires Cl (hydrolysable) 15.10%.

ω-Chloro-p-tolylphenylketone. (Thorner, Annalen, 1877, 189 84).

A slight modofication of Thorner's method had to be made since p-tolylphenylketone is obtained in a much purer state when made from toluene and benzoyl chloride by the Friedel-Craft reaction. The reactions are summarised as under.

$$CH_3.C_6H_5 + C_6H_5COCl \xrightarrow{AlCl_3} CH_3.C_6H_4.CO.C_6H_5 \xrightarrow[110°C.]{Cl_2} CH_2Cl.C_6H_4.CO.C_6H_5.$$

p-Tolylphenylketone (Bourcet, Bull. Soc. Chim. 1896, 945).

Benzoylchloride (50 gms.) was added slowly to a mixture of 25 gms. $AlCl_3$ in 330 c.c. toluene.

When all the benzyl chloride had been added the reaction mixture was heated to boiling until no more hydrogen chloride was evolved. The dark red liquid was poured into a large excess of water, the toluene layer separated, washed twice with dilute NaOH and dried over $CaCl_2$. Toluene was then distilled away from the ketone until the volume of the liquid left was about 90 c.c. This residue was cooled in ice when the p-tolylphenylketone separated out in a bright red mass which was filtered off and washed with a small quantity of light petroleum (b.p. 60-80°C) when most of the colour was removed. The ketone was then recrystallised from hot light petroleum (b.p. 60-80°C.) from which it separated in clear rhombic prisms of m.p. 59-60°C. The yield was 50% of that expected.

ω-Chloro p-tolylphenylketone.

This compound was prepared by a method analogous to that employed for the preparation of the meta isomer. The ω-chloro-p-tolylphenylketone was recrystallised from absolute alcohol from which it separated in rectangular plates of m.p. 96-97°C. Found: Cl (hydrolysable) 15.11%. $C_{14}H_{11}OCl$ requires Cl (hydrolysable) 15.10%.

Isomeric iodoanilines. (Baeyer, Ber., 1905, 38 2760-2762).

A slight modification of the method given in the above reference had to be used since it was found that better yields were obtained when the reduction

of the iodonitrobenzene was carried out according to the method of R.W. West (J.C.S., 1925, 127 494). The reactions are summarised as follows:-

$$NO_2.C_6H_4.NH_2 + NONO + H_2SO_4 \longrightarrow NO_2.C_6H_4N_2SO_4H.$$

$$NO_2.C_6H_4.N_2SO_4H + KI + I_2 \longrightarrow NO_2.C_6H_4I$$

$$NO_2.C_6H_4I \xrightarrow{Fe + HCl} NH_2.C_6H_4.I.$$

Isomeric iodonitrobenzenes.

The nitraniline (100 gms.) was mixed with 1000 c.c. water in a two litre beaker, 600 gms. conc. H_2SO_4 slowly added and the clear solution so obtained was quickly cooled to +5°C. and diazotised, the temperature being maintained between +5° and +10°C. The diazotised liquid was then added in small portions to a solution of 200 gms. KI and 200 gms. iodine in 200 c.c. water and the whole warmed for some time on the steam-bath after which excess iodine was removed with sodium bisulphite solution. The iodonitrobenzene crystallised out on cooling when it was washed with water and dried on a porous plate. In each case the yield was 90% of that expected. The m.p. of o-iodonitrobenzene was 49.5°C, that of m-iodonitrobenzene 35°C. and that of p-iodonitrobenzene 171.5°C.

Isomeric iodoanilines.

For each grammolecule of nitro compound, 500 c.c. alcohol and 10 c.c. conc. HCl were added. The solution, in a litre flask fitted with a reflux condenser, was heated to boiling on the steam-bath and 170 gms.

iron filings added in four portions, five minutes being allowed between each addition, and the whole boiled vigorously for 3 hours. The hot liquid was then filtered, the iron residue washed with a little hot alcohol and the filtrate transferred to a large flask where it was steam-distilled. As the amines are very soluble in alcohol the first portion of the distillate, which was mainly alcohol, was rejected. The amines were purified by conversion to the hydrochloride which was dissolved in water and extracted with ether; this removed any unchanged nitrobenzene. The aqueous layer was separated off and the amine was precipitated with alkali. Para and ortho iodoanilines were recrystallised from light petroleum (b.p. 60-80°C.) from which they separated in white prismatic needles. m-Iodoaniline was distilled under reduced pressure and had b.p. 145.4°C at 13 mm. o-Iodoaniline had m.p. 60-61°C., m-iodoaniline had m.p. 27°C. and p-iodoaniline had mp.67-68°C.

Isomeric iododimethylanilines. (Baeyer, Ber., 1905, 38 2762).

The ortho-derivative was prepared by the direct methylation of iodoaniline with dimethyl sulphate, the meta, by the distillation of m-iodophenyltrimethylammonium-iodide, and the para, by the direct iodination of dimethylaniline.

o-Iododimethylaniline.

The reactions are summarised as follows:-

$$o\text{-}I.C_6H_4.NH_2 + (CH_3)_2SO_4 \longrightarrow (o\text{-}I.C_6H_4.NH\,CH_3)^{+}(CH_3SO_4H)^{-}$$

$$\downarrow \text{NaOH.}$$

$$o\text{-}I.C_6H_4.NHCH_3 + CH_3SO_4Na$$

$$o\text{-}I.C_6H_4.NH.CH_3 + (CH_3)_2SO_4 \longrightarrow (o\text{-}I.C_6H_4.N(CH_3)_2)^{+}(CH_3SO_4H)^{-}$$

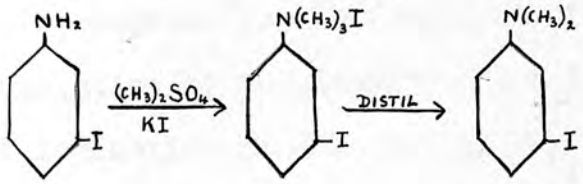
$$\downarrow \text{NaOH}$$

$$o\text{-}I.C_6H_4.N(CH_3)_2 + CH_3SO_4Na.$$

o-Iodoaniline (60 gms.) was mixed with 60 gms. water and one molecule of dimethylsulphate added, the whole being shaken from time to time and cooled in water. When all the amine had dissolved the reaction mixture was neutralised with NaOH and a second molecule of dimethylsulphate added. The mixture was again shaken and cooled until all the oil had disappeared, neutralised with NaOH, and a third molecule of dimethylsulphate added to ensure full methylation. After the oil had passed into solution for the third time the acid liquid was brought into a solution of 150 gms. $K_4Fe(CN)_6$ and 90 gms. conc. H_2SO_4 in a litre of water and the white crystalline precipitate so obtained filtered off and washed with water. On addition of NaOH to this compound o-iodoaniline was precipitated as an oil which was extracted away with ether and the ethereal layer dried over solid NaOH. The ether was then evaporated away from the oil which was distilled under reduced pressure and had b.p. 116°C. at 11 mm.

m-Iododimethylaniline.

m-Iodoaniline is readily converted to m-iodophenyltrimethylammoniumiodide by the action of dimethylsulphate and potassium iodide. This quaternary salt, when distilled under reduced pressure is converted into m-iododimethylaniline. The first stages of the reaction are identical to those used for the preparation of o-iododimethylaniline, the subsequent reactions are summarised as follows:-



m-iodoaniline (1 mol.) was mixed with 2½ times its weight of water in a stoppered bottle; dimethylsulphate (1 mol.) added and the whole well shaken until all the oil had gone into solution. The solution was now neutralised with NaOH and the above process repeated first with one molecule then with one and a half molecules of dimethylsulphate. After the solution had been neutralised for the third time it was shaken up with potassium iodide when m-iodophenyltrimethylammoniumiodide separated out. This was filtered off and dried thoroughly on a porous plate. Fifty grams of the quaternary iodide were put into a claisen flask, the pressure reduced to 12 mm. and the temperature raised slowly. The decomposition was carried out with great caution otherwise tar products were formed. The quaternary salt gradually became liquid

when it was distilled and the fraction boiling between 140° to 145°C. at 12 mm. collected. This fraction was redistilled and had b.p. 142-145°C. and it solidified several weeks after its preparation when it had m.p. 37°C. (Baeyer, loc.cit. m.p. 38-39°C). Found: I; 51.09; $C_8H_{10}NI$ requires I, 51.4%.

p-Iododimethylaniline. (Baeyer, loc.cit.; Weber, Ber., 1877, 10 765).

This compound is not readily prepared by the direct methylation of p-iodoaniline but is formed by the direct iodination of dimethylaniline in good yields. Weber used a solution of dimethylaniline in carbondisulphide but Baeyer found glacial acetic acid to be the better solvent. The reaction is summarised as follows:-

$$2\ C_6H_5N(CH_3)_2 + I_2 \longrightarrow 2\ p\text{-}I.C_6H_4.N(CH_3)_2$$

Iodine (200 gms.) added to a solution of 100 gms. dimethylaniline in 500 gms. glacial acetic acid in a stoppered bottle was mechanically shaken for two days. The reaction mixture was poured into water and the black mass so obtained filtered off and washed with water. This solid was dissolved in alcohol, decolourised with sodium thiosulphate and reprecipitated by the addition of water. p-Iododimethylaniline was finally recrystallised from light petroleum (b.p. 40-60°C.) from which it separated in colourless plates of m.p. 82°C.

Isomeric iodophenyltrimethylammoniumiodides.

o-Iodophenyltrimethylammoniumiodide.

This compound was prepared by a method analogous to that employed for the preparation of the meta derivative (q.v.p. 44). In this case the methylation took place much more slowly and the yield was poor. The compound isolated was recrystallised from water from which it separated in rectangular prisms which melted and decomposed at 161-162°C. Found: I (hydrolysable) 32.51% . $C_9H_{14}.N\,I_2$ requires I (hydrolysable) 32.65%.

m-Iodophenyltrimethylammoniumiodide. (Baeyer, loc.cit.)

This compound was obtained in the preparation of m-iododimethylaniline (q.v.p. 44). It was recrystallised from hot water from which the meta quaternary iodide separated in rectangular prisms which melted and decomposed at 158-159°C. Found: I (hydrolysable) 32.40% $C_9H_{14}N\,I_2$ requires I (hydrolysable) 32.65%.

p-Iodophenyltrimethylammoniumiodide.

p-Iododimethylaniline (20 gms.) along with 12 gms. methyl iodide was sealed up in a thick glass tube and heated in the steam-bath for one hour. At first the amine dissolved in the methyl iodide but crystals of the quaternary iodide soon appeared and finally the reaction mixture was quite solid. This solid was recrystallised from hot water from which the para

quaternary iodide separated in rectangular prisms which melted and decomposed at 212°C. Found: I (hydrolysable) 32.6%. $C_9H_{13}NI_2$ requires I (hydrolysable) 32.65%.

Meta and para iodophenyltrimethylammoniumchloride.

These compounds were each prepared by the action of moist silver oxide on a solution of the quaternary iodide in water which gave a solution of the quaternary hydroxide. This solution was acidified with HCl and evaporated to dryness when the quaternary chloride thus obtained was almost pure. Several attempts were made to prepare the ortho derivative but it could not be isolated. The reactions are summarised as follows:-

$$I.C_6H_4.N.(CH_3)_3I \xrightarrow{AgOH} I.C_6H_4.N(CH_3)_3OH \xrightarrow{HCl} I.C_6H_4.N(CH_3)_3Cl.$$

Sodium hydroxide (12.4 c.c. of 2 N) was added to a solution of 4.2 gms. $AgNO_3$ in 20 c.c. water and the precipitate filtered off and washed well with water. The iodophenyltrimethylammoniumiodide was dissolved in 50 c.c. water,(this was warmed if necessary) and the silver oxide, prepared above, added. The mixture was well shaken and the reaction was ended when the dark brown silver oxide had all been converted to the pale yellow iodide. The solution was cooled, filtered, the filtrate acidified with conc.HCl and evaporated to dryness. The resulting quaternary chlorides were recrystallised from an alcohol ether mixture.

m-Iodophenyltrimethylammoniumchloride melted and decomposed at a temperature of 209°C. Found: Cl (hydrolysable) 11.80% $C_9H_{14}N$ I Cl requires Cl (hydrolysable) 11.93%. p-Iodophenyltrimethylammonium-chloride melted and decomposed at 200°C. Found: Cl (hydrolysable 11.93%. $C_9H_{14}N$ I Cl requires Cl (hydrolysable) 11.93%.

These compounds were both slightly deliquescent.

3-Nitro-p-tolylbenzoate.(Allsop,Kenner,J.C.S.,1923,2314).

Benzoylchloride (1 mol.), m-nitrocresol (1 mol.) and sodium hydroxide solution (1 mol.) were heated together onthe steam-bath for two hours with agitation. The reaction mixture was then cooled when a solid separated out. This was filtered off, washed with water and recrystallised from alcohol from which 3-nitro-p-tolylbenzoate separated in prisms of m.p. 100-101°C.

3-Nitro-p-tolylbenzylether.(Fischer,Annalen,1884,224,142).

m-nitrocresol (5 gms.) dissolved in 10 c.c. alcohol was added to a solution of 3 gms. NaOH in 10 c.c. alcohol and 3 c.c. water. Benzylchloride (4 gms.) was added slowly with shaking and the mixture was heated on the water bath for 2 hours. The solution was then poured into water and the white solid so obtained filtered off, washed with water, dried and recrystallised from light petroleum (b.p. 40-60°C) from which it separated in needles of m.p. 53-54°C.

3-Nitro-p-tolyl-*m*-nitrobenzoate.

m-Nitrocresol (3 gms.) was dissolved in 10 c.c. alconol and a solution of 3 gms. NaOH in 3 c.c. water and 10 c.c. alconol added. m-Nitrobenzoyl-chloride (3 gms.) was added and the solution was heated on the steam-bath for two hours. The 3-nitro-1-tolyl 3'-nitrobenzoate was isolated in the same way as was 3-nitro-1-tolylbenzoate and recrystallised from acetone from which it separated in prisms of m.p. 141-142°C. FoundN; 9.3 $C_{14}H_{10}O_6N_2$ requires N, 9.37%.

2-Nitro-p-tolyl-*m*-nitrobenzoate.

This compound was prepared in the same way as the 3-nitro derivative using o-nitrocresol instead of m-nitrocresol. Prisms m.p. 135-136°C. Found N; 9.35 $C_{14}H_{10}O_6N_2$ requires N, 9.37%.

EXPERIMENTAL.

I. Hydrolysis of ω - ω'-dichloro-di-p-tolylcarbonate (A), ω-chloro-p-tolylbenzoate (B), ω-chloro-p-tolylbenzyl-ether (C) and benzylchloride D at 76°C.

A weighed quantity of the substance (0.2 gm.) was dissolved in 90 c.c. absolute alcohol and 10 c.c. distilled water, in a 100 c.c. flask, and the volume made up to 100 c.c. with alcohol. The flask was immersed in a thermostat (76°C.) and aliquot portions removed at definite intervals of time (t), diluted with water, extracted with ether and the acid in the aqueous layer (representing the percentage change (x)) estimated by titration with standard alkali.

Compound:-	A	B	C	D
wt. of compound:-	0.2146 gm.	0.2153 gm.	0.2030 gm.	0.2170 gm.
t (in hours).	X	X	X	X
½	8.1%	11.4%	98.5%	
1	12.5%	23.1%	99.7%	10%
2	27.9%	43.0%	-	14.2%
4	45.1	72.1	-	22.5%
1/T = R	0.235	0.417	∞ approx.	0.088

T is the time in hours required to hydrolyse 50% of the compound.

The above results are expressed in Graph I p.14.

II. The hydrolyses of the isomeric ω-chloro-p-tolyl-nitrobenzoates were carried out as in the previous experiments.

Compound.	ortho-isomeride	meta isomeride	para isomeride
Wt.of Compound.	0.2074 gm.	0.2172 gm.	0.2498 gm.
t (in hours)	X	X	X
½	3.94%	5.65%	9.9%
1	8.30"	11.30"	17.8"
2	13.80"	19.60"	31.5"
4	23.90"	34.00"	56.0"
1/T = R	0.108	0.160	0.286

These results are expressed in Graph II p. 15.

III. The hydrolyses of ω-chloro-p-tolylbenzylether and the isomeric ω-chloro-p-tolylbromobenzylethers were carried out in 10% aqueous alcohol at 25°C. but it was found better to estimate the amount of hydrochloric acid liberated by adding a standard solution of silver nitrate and back titrating with standard ammonium thiocyanate.

Compound	Unsub.	ortho isomeride	meta isomeride	para isomeride
wt.of compound.	0.1030 g.	0.1080 g.	0.1095 g.	0.1032 g.
t(in hours)	x	x	x	x
¼	19.1%	11.2%	11.5%	16.5%
½	30.0"	15.5"	18.7"	26.1"
1	47.5"	25.2"	30.3"	42.0"
2	71.0"	40.5"	49.1"	61.2"
1/T = R	0.934	0.370	0.424	0.833

The above results are expressed in Graph III p.16.

IV. The hydrolyses of ω-chloro-m-tolylphenylketone (A), ω-chloro-p-tolylphenylketone (B) and ω-ω'-dichloro-m-tolylcarbonate (C) were carried out at 76°C as in the examples quoted in I.

Compound	A	B	C
wt.of Compound	0.2094 g.	0.1982 g.	0.2115 g.
t (in hours)	x	x	x
½	2.50%	1.50%	4.2%
1	4.79"	3.42"	7.2"
2	7.76"	6.53"	10.4"
3	-	-	-
4	-	-	14.5"
5	14.00	12.4	-
1/T = R	0.045	0.040	0.042

1/T was arrived at by extrapolation. These results are expressed in Graph IV, p.17.

V. Hydrolyses of (A) and (B) at 100°C in 20% n-propyl alcohol.

Compound	A	B
Wt.of Compound		
t (in hours)	x	x
1	13.1%	8.5%
2	21.3"	15.0%
4	37.5"	24.9"
6	54.7"	34.8"
1/T = R	0.180	0.120

These results are expressed in Graph V, 18.

VI. The hydrolysis of meta and para nitrobenzyl-bromide, in N/50 NaOH was carried out as follows. A weighed quantity (0.25 gm.) of the nitrobenzyl bromide was dissolved in 90 c.c. absolute alcohol and 10 c.c. N/5 NaOH in a 100 c.c. flask, and the volume made up to 100 c.c. with alcohol. The flask was immersed in a thermostat (25°C) and aliquot portions removed after definite intervals of time, diluted with water, 10 c.c. N/10 HCl added, the whole extracted with ether and the aqueous layer titrated with N/10 NaOH. In order to estimate the amount of hydrolysis a blank experiment was performed, that is, in a 100 c.c. flask were added 90 c.c. absolute alcohol, 10 c.c. N/5 NaOH and the volume made up to 100 c.c. with alcohol. The flask was immersed in tche thermostat (25°C) for one hour, 10 c.c. of the solution removed and treated as above. In this way the true volume of NaOH required is equal to the difference between the volume used and the volume used in the blank.

The hydrobromic acid formed was estimated at the same time by method of Volhard. In this way an estimation of the percentage course of the reaction was made (i) according to the amount of alkali used and acid produced (ii) to the amount of halogen acid produced.

The results obtained are expressed in Graph VI p. 19.

Compound	meta isomeride		para isomeride	
Wt.of Compound	0.2490 g.		0.2488 g.	
t (in hours)	x_a	x_n	x_a	x_n
1	29.5%	41%	38.4%	43%
2	47.8"	56.9%	59.5"	81.1%
4	66.7"	89.7"	79.0"	95.2"
7	84.2"	99.8"	93.5"	99.4"

A similar experiment was carried out using N/10 NaOH solution.

Compound	meta isomeride		para isomeride	
Wt.of Compound	0.2643 g.		0.2488 g.	
t (in hours)	x_a	x_n	x_a	x_n
$\frac{1}{4}$	50.9%	55.6%	66.6%	51.9%
$\frac{3}{4}$	80.4"	85.5"	92.7"	92.0"
$1\frac{3}{4}$	105.6"	99.4"	117.6"	97.2"
$3\frac{3}{4}$	124.0"	100.2"	122.2"	99.4"
$5\frac{3}{4}$	129.5"	100.1"	129.6"	99.4"

x_a corresponds to the percentage change calculated from the amount of acid produced.

x_n is the percentage change calculated on the amount of halogen liberated.

VII. The hydrolysis of meta and para ω-bromotoluic-acid was carried out by the same method as that used for the hydrolysis of the nitrobenzylbromides but in this case alkaline solutions of normalities N/20, N/100, N/250, N/500 were employed. No difference was observed between the two methods of estimation, that is, (1) estimation of alkali used up and (2) estimation of hydrobromic acid by method of Volhard.

	N/20 NaOH.		N/100 NaOH.	
Compound	meta isomer.	para isomer.	meta isomer.	para isomer.
Wt.of Compound	0.2030g.	0.1967g.	0.2009g.	0.2042g.
t (in hours)	x	x	x	x
½	19.3%	15.1%	34.2%	29.4%
1	28.1"	23.8"	51.3"	43,2"
2	40.7"	32.6"	62.7"	51.7"

	N/250 NaOH.		N/500 NaOH.	
Compound	meta isomer.	para isomer.	meta isomer.	para isomer.
Wt.of Compound	0.2053g.	0.1892g.	0.1619g.	0.2123g.
t (in hours)	x	x	x	x
½	37.2%	30.5%	45.5%	31.2%
1	55.1"	47.2"	69.1"	51.1"
2	76.6"	60.3"	92.3"	73.3"

These results are expressed in graph VII p.20.

Reduction.

(A) The liberation of iodine from o- and p-iodoanilines and the corresponding dimethyliodoanilines was carried out according to the method used by Nicollet and Sampey (J.A.C.S., 1927,49 1796 et.seque.). A weighed quantity (0.125 gm.) of the iodide was dissolved in 10 c.c. hot glacial acetic acid, in a 25 c.c. flask, 5 c.c. 10% hydrohcloric acid, containing 0.5 gm. $SnCl_2.2H_2O$, added and this solution heated on the steam-bath for the desired length of time, when the flask was cooled in water and the solution analysed for iodide by method of Fresnius (Treadwell and Hall, Analytical Chemistry, 1919 2 657). To the sample to be analysed was added 15 c.c. chloroform and then a 10% solution of $NaNO_2$ drop by drop, with thorough mixing, until the chloroform layer began to be coloured, when an additional 0.5 c.c. $NaNO_2$ solution was added. The chloroform layer was separated, the acid liquid extracted with two further 15 c.c. portions of chloroform and the combined extracts washed with several small quantities of water. After the addition of a few drops of sodium bicarbonate solution, the iodine in the chloroform layer was estimated by titration with 0.02N sodium thiosulphate.

Compound.	o-iodoaniline		p-iodoaniline	
t (in hours()	wt.of comp.	x	wt.of comp.	x
½	0.0995 gm.	32.5%	0.1283 gm.	17.5%
1	0.1025 "	57.1"	0.1210 "	35.7"
2	0.1080 "	86.8"	0.1075 "	61.1"

Iodine was not liberated from the m-compound.

Compound.	o-iododimethylaniline		p-iododimethylaniline	
t(in hrs.)	wt.of comp.	x	wt.of comp.	x
½	0.1102 gm.	29.3%	0.1779 gm.	15.0%
1	0.1025 "	49.8"	0.1123 "	30.5"
2	0.1163 "	82.5"	0.1210 "	58.8"

Iodine was not liberated from the m-compound.

(B) The same method was employed to see if iodine was liberated from the isomeric iodophenyltrimethylammoniumiodides. One atom of iodine was liberated in each case but this was due to the iodine attached to the nitrogen atom since the corresponding chlorides, m-iodophenyltrimethylammoniumchloride and p-iodophenyltrimethylammoniumchloride were unaffected by the reducing agent.

The above results are expressed in Graph VIII p. 21.

NITRATION.

p-Tolylbenzoate (25 g.) was dissolved in 50 c.c. glacial acetic acid and 6.5 g. HNO_3 (D = 1.4) in 10 c.c. glacial acetic acid added slowly, the temperature being maintained at 45°C. throughout the experiment. The solution was then poured into ice-water and the solid nitration product so obtained, filtered, washed with water and recrystallised from alcohol from which it separated in prisms of m.p. 100°C. The yield was 80% of that expected and this compound did not depress the m.p. of authentic 3:nitro-p-tolylbenzoate (see p. 48).

p-Tolylbenzylether (10 g.) was dissolved in 100 c.c. 100% H_2SO_4 and 3 gms. of HNO_3 (D = 1.4) in 9 c.c. 100% H_2SO_4 added slowly, the temperature being maintained at 10°C. throughout the addition. The solution was then poured over ice and the solid product so obtained filtered, washed with water and recrystallised from light petroleum (b.p. 40-60°C.) from which it separated in needles of m.p. 53-54°C. The yield was 90% of that expected and this compound did not depress the m.p. of authentic 3-nitro-p-tolylbenzylether (see p. 48).

p-Tolyl-m-nitrobenzoate was nitrated in the same way as was p-tolylbenzylether (above). The yield of nitro compound was 70% of that expected and it had m.p. 135-136°C. This compound did not depress the m.p. of authentic 2-nitro-p-tolyl-3'-nitrobenzoate (see p. 49.).

DISCUSSION.

The nitration of p-cresol ortho to the hydroxyl group receives a ready explanation on the principle of "induced alternate polarities" since the hydroxyl has long been recognised as a more powerful directing group than is the methyl group. (cf. for example Lapworth and Shoesmith, J.C.S., 1922, 121 1392; Shoesmith and Slater, J.C.S., 1924, 125 2278). At first sight the nitration of p-tolylcarbonate (Holleman, loc.cit.) would be deemed an example in which this principle gives no assistance since the (NO_2) group enters the molecule ortho to the (CH_3) and meta to the (-O-). The fact that tche oxygen is attached to the carbonyl group might have been expected to render the (-O-) a more negative "key atom" (i.e. $\bar{O}=\overset{+}{C}-\bar{O}-$)since the doubly bound oxygen is a negative key atom and the effect would be expected to be carried on to the (-O-) which itself acts as a negative key atom. As has already been mentioned (see p. 4) attack ortho to the (-O-) might be prevented by the proximity of the second benzene nucleus. This was proved to be improbable by the fact that in the nitration of p-tolylbenzylether, the (-O-) displayed its usual directive influence, as it also did in the case of p-tolylbenzoate, which however could not be nitrated under standard conditions.

The effect of the carbonyl group on reactivity.

Recent theories on the production of reactive positions in an organic molecule postulate the movement of electrons, which results in a different distribution of valency throughout the molecule. These can be briefly summarised as follows:-

(i) The movement of electrons might result from a repulsion from certain atoms or attraction by other atoms throughout the molecule, an effect relayed from atom to atom which results in the reactivity of all the atoms in the molecule being affected in the same way. This movement results in what has been called the "induced effect" (I), denoted by $\longrightarrow$ or $\longleftarrow$.

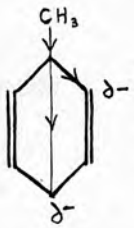
(ii) The electrons might also move in such a way that some positions in a molecule are rendered more or less reactive than others. This has been called a "tautomeric effect " (T), symbolised by $\curvearrowright$.

(iii) A hindering of reactivity owing to spatial considerations may be termed a steric effect and influences which pass through space and not along a series of atoms has been termed the "direct effect" (D).

This is a short summary of the views put forward, in the first place by Robinson,(J.C.S., 1926, 401) and later by Ingold (see especially Ann.Rep.1927, pp.106-119; 1928,pp.118-152) to whom the introduction of the symbols I,T and D is due. It is interesting to note that the effects were described by Lapworth as "general" (i.e.I),"alternating"(i.e.T), and "steric"

although some of the effects quoted as being due to steric hindrance are probably due, in part, to the direct effect (D). The difference between the two effects being that the steric effect was ascribed as being due to the size of the atoms near to the position at which reaction takes place whereas the direct effect operates through space and affects reactivity in the same way as the general effect.

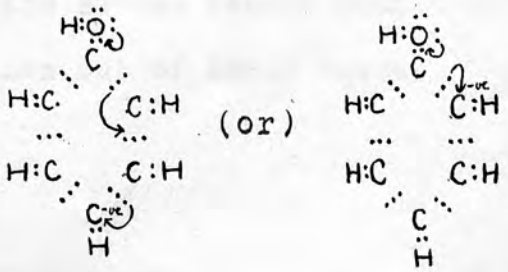
Toluene may be quoted as an example of the "induced effect"



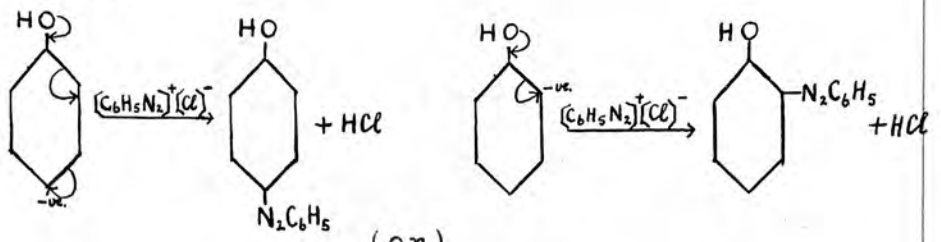
∂-indicates a small negative charge.

passed direct to the o- and p- positions because of the electron repelling effect of the (CH_3) group (see p. 2) which results in the appearance of an excess of electrons on the o- and p- carbon atoms. (This is the suggestion put forward by Ingold (Rec.trav. Chim.,1929,48 805) who assumes the Dewar formula for toluene. A similar transmission of electronic effects was put forward earlier by Robinson (loc.cit.).

In phenol the excess of electrons in the o- and p- positions can appear by a different mechanism such as is illustrated below, the arrows denoting the movement of electrons.



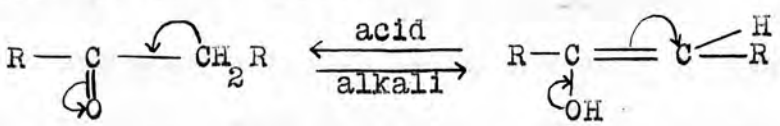
The movement of electrons commences, at the moment of reaction from the oxygen atom, in virtue of the presence of a number of uncombined electrons at this point. This results in the appearance of a negative charge on the o- and p-carbon atoms but never on the m-carbon atom. The importance of the appearance of this negativity is shown expecially by the attraction of the positive diazonium ion in the diazo coupling of phenols.



(or)

The reaction ends with the expulsion of the (H) attached to the negative carbon atom, to combine with the negative chlorine ion with production of hydrochloric acid. This suggestion is due to Robinson (J.S.C.I.,1925,426).

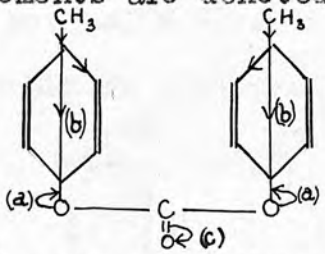
The movement of electrons in the carbonyl ($>C=O$) group is postulated as moving in such a way that the ($=O$) acquires more electrons than the carbon. For example the tautomeric keto-enolic transformation can be represented as follows:-



in which the arrows denote displacement of electrons, none of them out of their octet. The acquisition of

electrons by the oxygen atom is a powerful driving force and results in a deficiency of electrons on the carbon atom in the carbonyl group, and a production of a positive charge at that point. Thus the carbonyl group can function as a dipole (see p.4) and to the positive end of this electrons are attracted.

In the case of p-tolylcarbonate the repulsion of electrons from the (-O-) is counteracted by the attraction due to the (>C=O) grouping. The electronic movements are denoted as follows:-



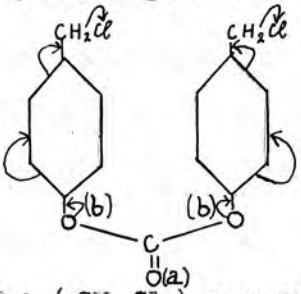
from which it is seen that the position ortho to the (CH_3) would be expected to be more reactive than in the case of p-cresol. The (CH_3) groups, by process (b) and the (>C=O) group, by (c) all direct against the movement of electrons from the (-O-), process (a), the normal directing influence in the nitration of p-cresol. The tendency of the singly bound oxygen atoms to neutralise each other must also be very appreciable and is quite conceivable from a study of the diagram. This is borne out in the nitration of p-tolylbenzoate which would have been expected to nitrate in the same position as in the case of p-tolyl-carbonate, that is, with the (NO_2) group o- to the

(CH_3), whereas it entered the position o- to the (-O-) atom.

Hydrolysis of ω-ω'-dichloro-di-p-tolylcarbonate and ω-chloro-p-tolylbenzoate.

The hydrolyses of the benzyl chlorides are reactions closely connected with the phenomenon of substitution in the nucleus of benzenoid derivatives. This connection was very clearly shown in the case of the above compounds (see table I p. 50). The diagram of electronic movements in ω-ω'-dichloro-di-p-tolylcarbonate may be represented as follows.

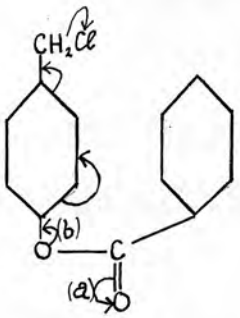
I



(The effect of the (CH_2Cl) groups is such as would neutralise to some extent the movement of electrons due to the (-O-) atoms, but it would be the same in all the chlorides discussed and its effect can therefore be neglected).

The above diagram shows the movement of electrond to the (Cl) atom when there is a source from which they can be obtained (process (b)), and the withdrawal of electrons by the ($\geq$C=O) group (process (a)). The diagram representing the electronic movement in the case of ω-chloro-p-tolylbenzoate is as follows.

II.



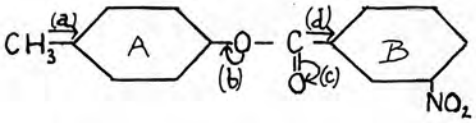
The movements (a) and (b) in case (II) are similar to those in (I). For comparative purposes the reciprocal of the time in hours ($I/T_t = R_t$) taken to hydrolyse 50% of the substituted benzyl chlorides was calculated. In the case of ω-ω'-dichloro-di-p-tolylcarbonate (I), $R_{76°}$ was found to be 0.235 and for ω-chloro-p-tolyl-benzoate (II), $R_{76°}$ was found to be 0.417 (see table I, p.50). The decrease in reactivity of the chlorine in (I) as compared with that in compound (II) may be due to the tendency of the (-O-) atoms in (I) to neutralise each other, an effect which is absent in (II).

Hydrolysis of ω-chloro-p-tolylbenzylether.

In this compound there is no withdrawal of electrons due to the ($\geq$C=O) group, as in the above cases, and the chlorine is very labile; $R_{76°} = \infty$ (approx.) (see table I, p.50) and $R_{25°} = 0.934$ (table III, p.51). Here, as in the case of the methoxybenzylbromides (Shoesmith, loc.cit.) the (-O-) atom exerts its normal electron repelling influence. The isomeric methoxybenzylbromides are much more reactive compounds than ω-chloro-p-tolylbenzylether.

Hydrolysis of the isomeric ω-chloro-p-tolylnitrobenzoates and the nitration of p-tolyl-m-nitrobenzoate.

The reciprocals of the time taken to hydrolyse 50% of the ω-chloro-p-tolyl-o- and m-nitrobenzoates (table II, p.51) are smaller than that of ω-chloro-p-tolylbenzoate (table I, p.50), that is, in the case of the nitro derivatives, the directing influence of the (-O-) atom is neutralised (i) by the (>C=O) group; (ii) by a nitro group in the o- and m-positions in nucleus B (see below).

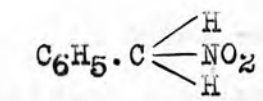


The diagram of electronic movements in the case of p-tolyl-m-nitrobenzoate is as shown above; (a) is the electronic repulsion from the (CH_3), (b) the tautomeric effect of the (-O-), (c) the electron withdrawal effect of the (>C=O) and (d) the general effect of the nitro group, which is similar to (c). Processes (a), (c) and (d) all tend to neutralise effect (b) that of the (-O-) which directs substituents ortho to itself. It would be expected that when p-tolyl-o- and m-nitrobenzoates are nitrated that the (NO_2) would enter the benzene nucleus in the position ortho to the (CH_3) and this was found to take place in the case of p-tolyl-m-nitrobenzoate. During nitration p-tolyl-

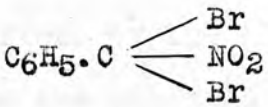
o-nitrobenzoate was hydrolysed and therefore no definite conclusions could be drawn from the results.

Hydrolysis of the isomeric ω-chloro-p-tolylbromobenzylethers.

The fact that the rates of hydrolysis of the isomeric ω-chloro-p-tolylbromobenzylethers are slower than that of ω-chloro-p-tolylbenzylether (table III, p. 51) is due to the electron attraction of the bromine atom and thus the order is o-Br < m-Br < p-Br < unsubstituted. Another example of the electron affinity of the bromine atom, which results in the slow rates of hydrolyses quoted, has been given by Baker and Ingold (J.C.S., 1926, 2462) who have proved that the introduction of bromine in place of the hydrogen atoms of the m-orienting group $-CH_2NO_2$ increases the amount of m-substitution in a nucleus to which the $-CH_2NO_2$ group is attached. Meta substitution is considered as due to the electron attraction of the bromine atoms. This is illustrated as follows:-



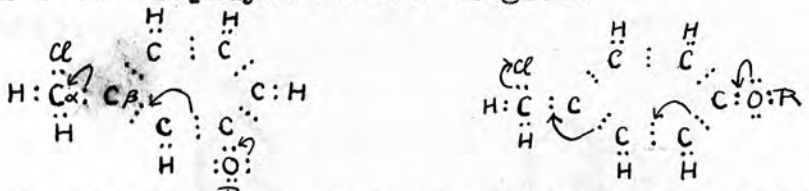
(meta-subs. 50%)



(meta-subs. 84%)

It is interesting to note that the activating of the chlorine in the bromo and nitro chlorides discussed in the preceding paragraphs, approaches nearer to the unsubstituted compounds the further the substituent (Br or NO_2) is removed from the reacting atom (side chain halogen).

The influence of the (-O-) atom in the ω-ω'-dichloro-di-m and p-tolylcarbonates is paralleled by that of the same atom in the methoxybenzylbromides from which the bromine was removed in the order:- m-<benzylbromide<p- (cf. J.C.S.,1922,121. 1398; J.C.S., 1926,127, 121). In the case of the carbonates the order of reactivity is m-<benzylchloride<p-. This is due to the transmission of the tautomeric effect from the singly bound oxygen attached to the nucleus in the case of the para compounds, an effect which is not passed to the meta positions in either series as displayed in the diagram.

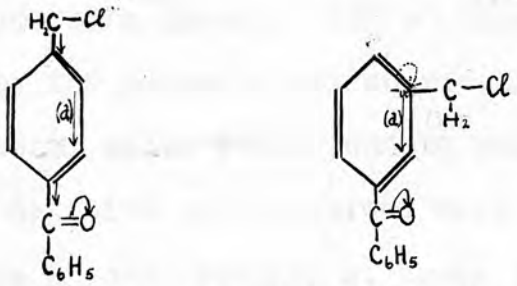


It is seen that in the meta compounds electronic shifts would result in combination between C atoms α and β by one electron which is improbable.

<u>The effect of the (>C=O) group in ω-chloro-m- and p-tolylphenylketones.</u>

In these ketones the effect of the (>C=O) is to attract electrons away from the chlorine atom and hence the rate of removal of the halogen is more difficult to accomplish in both cases than from unsubstituted benzyl chloride (table V, p.52,table I, p.50). The difference in the rate of removal of halogen from benzyl halides which contain a m-directing group with a strong inductive effect is as difficult to explain as that of m-substitution in compounds such as nitrobenzene etc. It might however be explained

in the following way. In the case of the p-compound the electrons are attracted from the chlorine atom and hence the chlorine is more difficult to remove than from the unsubstituted compound. The slight increase in the ease of removal of the halogen noted in the case of the m-compound could be due to a slight shift of electrons from between the m- and p-carbon atoms with production of a negative centre in the position meta to the (>C=O) group. This effect is relayed from the m-position direct to the chlorine atom. The electronic changes are illustrated as follows:-



In the diagram process (a) represents direct attraction to the (>C=O) group whilst ↷ represents the small electron displacement which results in the m-chloride being more readily hydrolysed than the para.

<u>The effect of the carbonyl group on the rate of removal of side chain halogen when it is attached directly to the benzylchloride nucleus as compared with its influence when it acts on the nucleus through a singly bound oxygen atom.</u>

The rate of removal of halogen from ω-chloro-p-tolylbenzoate (A) is much greater than is that from

ω-chloro-p-tolylphenylketone (B) (See table I, p. 50, table IV, p. 52).

(A) 

(B) 

This can be explained by the fact that in (B) the (>C=O) group exerts a direct attraction on the benzylchloride nucleus which results in electrons being withdrawn from the side chain halogen which is thus rendered more positive and therefore more difficult to remove by hydrolysing agent. In (A) this effect is counteracted by the normal electron repelling influence of the (-O-) atom, which would tend to make the chlorine more negative and therefore more easily removed. From a consideration of these results and from data obtained by Shoesmith (loc.cit.) on the rate of hydrolysis of p-methoxybenzylbromide it is concluded that effect of the (-O-) atom in compounds such as (A) is greatly reduced by the presence of the (>C=O) group but it is by no means entirely neutralised.

The alkaline hydrolysis of m- and p-nitrobenzylbromides.

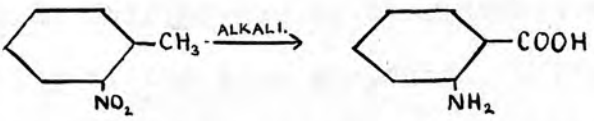
The hydrolyses of these compounds were carried out in alkaline solution in order to see if any difference existed between the order of activity in alkaline and acid reagent. There was a marked difference in that in alkaline solution the order was

m<p (see table VI p.54) not m>p, the order of reaction in acid hydrolysing agent (cf. J.C.S., 1924, 125 1313). The reaction which takes place in alkaline solution is not merely that represented by the equation:-

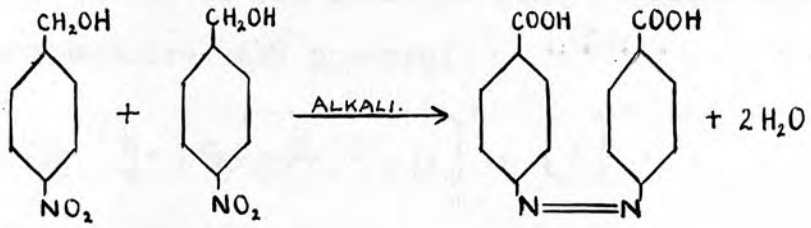
$$NO_2.C_6H_4.CH_2Br + NaOH \longrightarrow NO_2.C_6H_4.CH_2OH + NaBr.$$

because the amount of acidic compounds produced during these hydrolyses was discovered to be more than could be accounted for by the separation of one molecule of hydrobromic acid from each molecule of the nitrobenzyl-bromide.

Bergmann and Hervey (Ber., 1929, 62 B 893) have recently found that the action of alkali on p-nitrobenzylchloride led to the production of p-p'-dinitrostilbene but this does not fully explain the results obtained above. The production of acid from a nitro compound appears similar to the well known production of anthranilic acid by the action of alkali on o-nitrotoluene (Preuss and Binz, Z. ang. Ch., 1900, 16 385).



It is not suggested that in the case of the nitrobenzyl-bromides that the compound produced is anthranilic acid but the conversion of p-nitrobenzylalcohol to p-p'-azobenzenedicarboxylic acid could take place according to the following scheme:-



The investigation of this reaction is worthy of further notice.

<u>The hydrolyses of the m- and p-ω-bromotoluic acids in alkaline hydrolysing agent.</u>

These hydrolyses were carried out in order to see if a reversal of the order of reactivity could be brought about. The aim of the experiment was to produce ions of:-

$CH_2Br.C_6H_4.COO^-$ and Na^+

but no difference in the order of reactivity from that discovered in acid solution was observed (see table VII , p. 55).

<u>The reduction of various iodo derivatives of aniline.</u>

The removal of iodine from the o- and p-iodo derivatives of aniline was to be expected as was the non-reactivity of the meta compounds. This is in agreement with the results obtained by the action of hydriodic acid on the isomeric iodo and bromophenols (J.C.S., 1924, <u>125</u> 1314). The introduction of a group which exists as a positive pole, into the iodinated molecule had the effect of making <u>all</u> the nuclear iodine atoms non-reactive to reducing agent. The

induced effect (I) of the positive pole in these compounds is therefore very powerful.

$$\left[\text{I}.\ \text{C}_6\text{H}_4.\text{N}.(\text{CH}_3)_3\right]^+ . \left[\text{I}\right]^-$$

The seat of the positive pole is at the nitrogen atom. In the case of iodoaniline and iododimethylaniline the (N) atom acts as an electron source whereas in the iodophenyltrimethylammoniumiodides the (N) atom acts as an electron attractor.

SUMMARY.

1.

Investigations have been carried out with a view to discovering to what extent the influence of the oxygen atom in p-cresol is neutralised by (a) a ($\geq C=O$) group, (b) a (NO_2) group, (c) a Br atom when the two latter are situated at some distance from this oxygen atom.

2.

Advantage has been taken of the fact that there is a close connection between the ease of removal of halogen from compounds containing a CH .Hal.group and direct substitution in the benzene nucleus to which this group is attached.

3.

The alkaline hydrolysis of the nitrobenzyl-bromides gives an abnormal result because of the production of a secondary reaction. This was not observed in the case of the ω-bromotoluic-acids.

4. It has been shown that the conversion of the nitrogen atom in an amino group to one which has a positive charge in a substituted amino group prevents the removal of an iodine atom from any position in the nucleus to which the nitrogen is attached.

5.

It has been shown that a ($>C=O$) group directly attached to a benzylchloride molecule represses the ease of removal of the halogen atom very markedly.

6.

An attempt has been made to explain all the phenomena observed from the standpoint of the recent theories on reactivity in an organic molecule.
